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AMERICAN HEALTH CONSULTANTS

April 2003 • Volume 18, Number 4 • Pages 41-52

IN THIS ISSUE

Inserted in this issue:
2003 *AIDS Alert* Reader Survey

Results of VaxGen vaccine raise hope, controversy

The first AIDS vaccine to complete human trials showed disappointing results, even as VaxGen pledges to go forward with more studies. While researchers were encouraged by preliminary data showing that the antibody response to the vaccine offered some protection, AIDS groups criticized the company for putting a positive spin on the findings . . . . . Cover

10th Retrovirus Conference highlights

As new antiretroviral drugs near FDA approval, treatment strategies are focusing more intensely on the long-term benefits and risks of treatment as patients live longer and face new health problems. Long-term side effects were on the minds of many researchers, especially the impact of antiretroviral drugs (particularly protease inhibitors) on cardiovascular disease. 45

States and cities cut AIDS services in budget crisis

The federal government's FY 2003 budget provides modest increases in HIV prevention and care funding. Meanwhile, budget problems at city and state health departments mean reductions in AIDS programs, including critical services, such as drug treatment, nutrition, and housing assistance 47

In This Issue **continued on next page**

VaxGen vaccine trial fails the test but may offer insights

Presentation of data draws criticism as 'premature'

AIDSVAX, the first AIDS vaccine to complete human trials, showed disappointing results, with only a 3% protection rate. However, researchers were encouraged by preliminary data showing that the antibody response to the vaccine offered protection, particularly in a subgroup of African-Americans and Asians.

"When all volunteers were analyzed, the vaccine did not appear to be effective," says **Michael Para**, MD, a principal investigator in the study. "On the other hand, the black/Asian subgroup did appear effective."

AIDSVAX reduced the rate of infection by 3.8% in people who received it compared to a control group that received placebo injections — far from the 70% minimum efficacy experts estimate is needed to gain approval for widespread use.

VaxGen officials had said an efficacy of 30% might be enough to make the product useful in some populations.

The vaccine appeared to be effective, however, in a subgroup of subjects, notably African-Americans. Among them, 2% who received the vaccine became HIV-infected, compared to 8.1% of the placebo group — a statistically significant difference.

When Asians and mixed-race volunteers were

(Continued on page 43)

In This Issue **continued from page 41**

Moving toward integrating HIV care and prevention

As a harbinger of more integration between HIV prevention and HIV care, two federal committees that advise the Department of Health and Human Services have merged into a single committee.The merger is a first step toward linking the best of both worlds — prevention and treatment — for the benefit of HIV-positive patients 49

Taking steps toward integration of STD and HIV services

The National Alliance of State and Territorial AIDS Directors and the National Coalition of STD Directors have published a report on STD/HIV integration that provides reasons for integration as well as steps that state and local jurisdictions can take to support integration. For instance, recent studies have demonstrated that being infected with an STD may make it 2 to 23 times easier to transmit HIV, depending on the specific STD 50

COMING IN FUTURE ISSUES

■ HIV testing results: A new protocol for routine HIV testing can increase testing yield in urgent care centers

■ Co-infection issues: How new treatments are making hepatitis C curable in half of HIV-positive patients

■ *AIDS Alert International:* How billions of dollars in new funding will be spent in developing countries, and how this will affect U.S. research

■ ADAPs faltering in some states: Long waiting lists, restrictions, and other problems cited as result of cash-poor state governments, stingier federal government

AIDS Alert® (ISSN 0887-0292), including **AIDS Guide for Health Care Workers**®, **AIDS Alert International®,** and **Common Sense About AIDS**®, is published monthly by Thomson American Health Consultants, 3525 Piedmont Road, Building Six, Suite 400, Atlanta, GA 30305. Telephone: (404) 262-7436. Periodicals postage paid at Atlanta, GA 30304. POSTMASTER: Send address changes to **AIDS Alert**®, P.O. Box 740059, Atlanta, GA 30374.

Subscriber Information

Customer Service: (800) 688-2421. Fax: (800) 284-3291. Hours of operation: 8:30 a.m-6:00 p.m. M-Th, 8:30-4:30 F EST. E-mail: customerservice@ahcpub.com. Web site: www.ahcpub.com.

Subscription rates: U.S.A., one year (12 issues), $467. Approximately 18 nursing contact hours or Category 1 CME credits, $467. Outside U.S., add $30 per year, total prepaid in U.S. funds. One to nine additional copies, $374 per year; 10 to 20 additional copies, $280 per year. For more than 20 additional copies, call customer service for special handling. Missing issues will be fulfilled by customer service free of charge when contacted within one month of the missing issue date. **Back issues**, when available, are $78 each. (GST registration number R128870672.)

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added to the group of blacks — a total of about 500 of 5,000 volunteers — the protective effect was nearly as strong.

While the findings in minorities could have worldwide implications, vaccine experts cautioned it was dangerous to jump to conclusions so early.

"Until the data is crunched and the analyses are finished, it is completely premature to determine whether or not AIDSVAX is truly effective for particular populations," says **Pat Christen**, executive director of the San Francisco AIDS Foundation.

The Gay Men's Health Crisis (GMHC) in New York City, the nation's oldest AIDS organization, criticized the company for putting a positive spin on the results and offering false hope, particularly to minority populations.

"Subset analyses are problematic in the best of cases. With small numbers of African-Americans and Asians in the trial and wide confidence intervals associated with the results, making any statements about efficacy in this subpopulation is grossly premature," says **Gregg Gonsalves**, director of treatment and prevention advocacy at GMHC. "VaxGen's assertions of its vaccine's efficacy among blacks are based on 13 infections in this population in a trial of more than 5,000 participants. The assertions about efficacy among Asians are based on only four HIV infections in the study."

Some AIDS researchers went beyond expressing disappointment in the results to call for new strategies in vaccine development. The results "require that we reassess our strategy of vaccine development," says AIDS Health Foundation president **Michael Weinstein**. "Clearly, work should continue where the trial showed promise, but the general results suggest that 20 years into this pandemic, we really need to stop and take a long, hard look at this issue."

The foundation's chief of medicine, **Charles Farthing**, MD, who doubts that a preventive vaccine can be developed any time soon, suggested more vaccine resources be shifted to providing antiretroviral therapy in poor countries.

In coming months, review of the data will focus on the robustness of the findings, particularly the efficacy reported in the subgroups. The enrollment in those groups was so small that a few more or less infections could have made the results insignificant. For example, there were only 13 infections among blacks.

"This data could have been all over the map," says one investment analyst. "Two patients in the black group could have completely changed the statistical significance of this study."

"Yes, you have to be skeptical," agrees **Phillip Berman**, PhD, VaxGen's senior vice president of research and development and inventor of the vaccine. "When you look at just the blacks, you are starting to talk about a few infections here and there. On the other hand, the antibody response in the people who were protected was clearly higher. Also, it looks like the vaccinated persons got infected with a different [strain of] virus than the placebo ones. And in the few people who were infected, you see better CD4 response and a little better viral suppression. So, yes, the numbers are small, but you start to get a consistent story in the analysis, so each of those things makes me increasingly comfortable with the small numbers. We are on a track."

Whatever the vaccine's future, AIDS organizations called the completion of the trial, which had to overcome substantial and unique ethical and regulatory hurdles, a feat in itself.

"We applaud VaxGen for showing that a Phase III trial is possible for an AIDS vaccine and for proving successful enrollment and retention of trial participants is possible," says Christen. "It is a remarkable and historic accomplishment."

Participation was high

A total of seven inoculations of the vaccine were given over three years to high-risk gay and bisexual men and female partners of injection drug users. At least 5,000 received one vaccination, and more than 4,500 completed the trial. The high level of participation and completion was "truly remarkable," Para added.

"We were disappointed the vaccine did not induce a reduction in all populations," says Para. "Certainly the vaccinated subjects didn't show a reduction in HIV infection. However, the differences in infection rates in the black/Asian subgroup was quite remarkable."

The trial analysis showed no real difference in efficacy by age, geographic location, education, and most importantly, sexual behaviors, in any groups, particularly in minorities, he points out.

The trial found no evidence that the vaccine caused any safety problems or enhanced susceptibility to infection, which were two main barriers to getting Food and Drug Administration (FDA) approval, Para notes.

Vaccine recipients had a slightly higher rate of

AIDSVAX B/B Trial Statistics

- Volunteers completing three doses: 5,009
- Placebo recipients: 1,679
- AIDSVAX B/B recipients: 3,330
- White volunteers: 4,185
- Hispanic volunteers: 326
- Non-white volunteers: 498
- Black volunteers: 314
- Annual study infection rate: 2.7%
- Approximate efficacy (after at least 3 primary doses):
  - — All volunteers: 3.8% (p-value = 0.76)
  - — Non-white volunteers: 67% (p-value < 0.01)
  - — Black volunteers: 78% (p-value < 0.02)

pain, swelling, and tenderness at the injection site compared to placebo recipients, he says.

A separate Centers for Disease Control and Prevention study indicated that volunteers did not increase their risk behaviors, and VaxGen's preliminary analysis of the trial data indicates that risk behavior was reduced in both the placebo and vaccine groups.

The history of the gp120 vaccine has been a rocky one, beginning with the National Institutes of Health's decision in 1996 not to fund a Phase III trial of the vaccine after "breakthrough" infections were reported in smaller trials. Undaunted, **Donald Francis**, MD, VaxGen's cofounder and one of the first public health experts to claim that AIDS was caused by a virus, reorganized and sought private backing to complete the trials.

"The results from this groundbreaking effort will provide new insights into HIV and hopefully pave the way to even more effective vaccines," Francis says.

Indeed, the vaccine may provide the first evidence in humans that antibodies from a surface protein vaccine correlate with the protection needed for an effective vaccine.

"The correlates of protection are going to be very important," says one vaccine researcher. "We are dying for that information."

The antibodies from the immune response to the vaccine were higher in the black and Asian volunteers. Likewise, they were higher in those who remained uninfected. Also, it appeared that those who were vaccinated and became infected had lower viral loads and higher CD4 counts than those infected in the placebo group — an indication that the vaccine may have a therapeutic effect as well, Para notes.

Curiously, white and Hispanic volunteers seemed to develop consistently lower levels of protective antibodies following vaccination. VaxGen intends to conduct additional analyses to confirm if there was a direct correlation between the level of antibodies and the prevention of infection.

"We're not sure yet why certain groups have a better immune response, but these preliminary results indicate that a surface-protein vaccine that stimulates neutralizing antibodies correlates with prevention of infection," says Para.

Among the factors the company will examine more closely are behaviors, geographic location, age, and sex.

"We need to investigate these and other possibilities before we can say it's a real difference," Berman says. "There also could be differences in virus infectivity and strain variation."

VaxGen is nearing completion of its Phase III trial in Thailand, which is testing a formulation of AIDSVAX designed to protect against HIV subtypes B and E. The company expects to announce results of that trial in the second half of 2003. Subtype E is prevalent in Southeast and East Asia and the Central African Republic. Unlike the AIDSVAX B/B trial, which tested the vaccine against sexual transmission of the virus, the trial in Thailand is testing the vaccine against infection acquired by injection drug use.

The results from that trial could provide additional answers and possibly support the findings from the U.S. trial. "It could provide confirmation of what we saw here," Berman says.

No timetable for FDA review

While it is almost certain the FDA would not approve the vaccine for use in the general population, it is possible that with further study and changes AIDSVAX could be licensed for the subgroups, making it the first time a vaccine was approved for a subpopulation only.

VaxGen officials would not predict how soon the FDA would complete analysis of the data, nor what it would make of the findings in the subgroup. One possibility is that further studies would be required in that group.

"It's our current objective to follow up on current formulation and do whatever additional studies are necessary for licensure," Berman says. "In parallel, we will look at factors that underlie differences in response and protection, and that may be formulation changes or other biotechnology changes."

The changes could range from enhancing the vaccine by adding more immune modulators and adjuvants to simply changing dosing and administration schedules. "We will be following all leads, including looking at the genetic backgrounds," Berman says.

Because the vaccine is relatively simple compared to other candidates, teasing out what works and what doesn't would be relatively easy, requiring 20 volunteers instead of 2,000.

"Having a single protein design gives us a simpler case to study than with a live organism or split vaccine," Berman notes. "We know exactly what is in the product. So the possibility to nail this is much higher than with older technologies."

Had AIDSVAX proved highly effective and headed for FDA approval, the company was ready to ramp up production of the vaccine at several new facilities and have it available by 2005.

Currently, VaxGen is also in the early stage of developing a vaccine against HIV subtype C, prevalent in sub-Saharan Africa, India, and China. The company is committed to developing increasingly effective formulations of AIDSVAX that target all HIV subtypes, says CEO **Lance Gordon**, PhD.

"We intend to continue development of this vaccine through licensure, including additional studies as necessary, for use in groups in which the vaccine demonstrated a significant reduction in infection," he says. ■

New therapy strategies focusing on long term

Drugs' impact on heart is debated

As several new antiretroviral drugs near Food and Drug Administration approval, treatment strategies are focusing more intensely on the long-term benefits and risks of treatment as patients live longer and face new health problems.

"What is happening now is clinicians are starting to get more creative in tailoring regimens to patients' concerns and lifestyles," says **Douglas Mayers**, MD, a researcher at Boehringer Ingelheim Pharmaceuticals in Ingelheim, Germany.

That was one of the louder take-home messages from the 10th Conference on Retroviruses and Opportunistic Infections, held Feb.10-14 in Boston. The conference was short on headline news, especially in the area of treatment. And while several new drugs are nearing FDA approval, most of the studies presented data on drugs that are several years away from reaching the market.

What most distinguishes these new drugs from existing treatment options is that they promise to make therapy not only more effective but simpler to take with fewer side effects.

Longer lives, new health problems

Long-term side effects were on the minds of many researchers, especially the impact of antiretroviral drugs (particularly protease inhibitors) on cardiovascular disease.

Friss Moller, MD, a researcher at the Copenhagen HIV Program, presented a study of 23,468 HIV-positive patients in Europe showing that the risk of having a heart attack while on medication increases 26% per year. Although the number of heart attacks was fairly low — 126 attacks, 36 of which were fatal — the study concluded that being on antiretroviral drugs meant a greater elevation in serum lipid levels.

The Copenhagen study was just one of numerous presentations at the conference showing significant increases in cardiovascular diseases now that patients on highly active antiretroviral therapy (HAART) are living longer. A study from Johns Hopkins University followed 6,711 HIV-positive patients for more than three years. Their risk for having a heart attack was twice as great if they were on protease inhibitors — a higher risk than from smoking cigarettes.

"What we are seeing at this conference is the rates of cardiovascular mortality are starting to go up in HIV patients as they live longer with the disease," Mayers says.

While some of the increase in disease is attributed to lifestyles of patients, many of whom are more likely to smoke and have other heart disease risk factors, some antiretroviral drugs are more risky than others, researchers note. Protease inhibitors, for example, pose the greatest risk because of their effect on increasing serum lipid levels, while non-nucleoside reverse transcriptase inhibitors (NNRTIs) have better lipid profiles.

Boehringer presented new data from its non-nucleoside reverse transcriptase inhibitor, nevirapine (Viramune), that included not only

efficacy on viral load but also its impact on cholesterol.

The data came from the first-ever large scale randomized trial directly comparing the safety of two NNRTIs — nevirapine and efavirenz — in combination therapy for HIV-positive drug-naive patients.[1]

While the two drugs appeared comparable with respect to viral suppression, Boehringer pointed out that nevirapine is not only cheaper than efavirenz, but had a better lipid profile. Specifically, it said patients in the nevirapine regimens experienced a greater increase (37%) in HDL-c ("good") cholesterol than those in the efavirenz regimen (24%) over 48 weeks.

"I think it is becoming increasingly important and obvious that you want to avoid that risk if you can, so I would always go for the drug that is going to give that increase, if you have the option," says **Joep Lange**, MD, lead investigator for the International Antiviral Therapy Evaluation Center and professor of medicine at the University of Amsterdam.

Bristol-Myers Squibb presented data suggesting that long-term therapy with its protease inhibitor atazanavir resulted in sustained virologic suppression. Moreover, patients switching to atazanavir from nelfinavir (another protease inhibitor) exhibited not only improved virologic suppression but also a significant decrease in serum lipid levels.

Data from the long-term, open-label observational switch study showed that patients who switched from nelfinavir to atazanavir for 24 weeks of treatment experienced improved virologic suppression and a clinically significant reduction of total cholesterol, LDL (bad cholesterol) and triglycerides.

Bristol-Myers Squibb recently submitted a new drug application to the Food and Drug Administration (FDA) for atazanavir, an azapeptide viral protease inhibitor of HIV-1. It is the first new application for a protease inhibitor to be submitted with pharmacokinetic data supporting the potential for once-daily administration.

VA study contradicts other findings

Not all data emerging on cardiovascular disease are showing increased risk. A new study of more than 36,000 patients treated for HIV at Veterans Affairs health care facilities from 1993 to 2001 found a steady drop in the rate of deaths and hospital stays due to vascular problems.

"Fears about vascular disease as a side effect of these drugs shouldn't keep patients and their doctors from using the best treatments available," says study leader **Samuel Bozzetta**, MD, an infectious disease specialist at the VA San Diego Health Care System.

The study, appearing in the Feb. 20 issue of the *New England Journal of Medicine*, may reassure doctors and patients who see benefits from HAART but worry about vascular complications, among other side effects.

As a caveat, however, Bozzetta warned that the study followed patients for only eight years, and that the findings may not reflect the seriousness of vascular disease with long-term HAART.

One problem is not knowing whether HIV itself can cause vascular disease. Indeed, some research has shown that HAART may protect against heart damage by suppressing the virus, he noted.

Other drugs in the pipeline

One of several new experimental drugs before the FDA is a enfurvitide (Fuzeon), a fusion inhibitor manufactured by Durham, NC-based Trimeris. A new class of drugs, fusion inhibitors block HIV from fusing with healthy cells. Enfurvitide is the furthest along in this family of drugs and is expected to receive FDA approval in March.

New data on an offspring of enfurvitide, T-1249, was presented at the conference.[2] The study showed that patients who had developed resistance while on enfurvitide experienced a 92% average reduction in viral load after switching to T-1249, which is several years behind development and will begin Phase II trials later this year.

Another first in a new class of drugs is Tipranavir, a non-peptidic protease inhibitor manufactured by Boehringer Ingelheim Pharmaceuticals. A Phase II study of the drug in highly experienced HIV-positive patients showed significant reduction in viral loads. Large studies evaluating different doses of the drug are beginning at more than 280 centers in North America, Europe and Australia.

"These preliminary results suggest that tipranavir may be a promising option for patients who have few or no treatment options because of drug resistance," says **Joseph Gathe**, MD, a researcher at Therapeutic Concepts in Houston.

The first clinical data on TMC114, a next-generation protease inhibitor, showed significant antiviral activity in multiple PI-experienced HIV patients currently failing PI therapy. In the 50-patient study, the median reduction in plasma viral load was -1.35 log10 copies/ml HIV-1 RNA after 14 days of treatment.[3]

TMC114 is being developed by Tibotec, a Belgian pharmaceutical research and development company.

"These early clinical results of TMC114 in highly treatment-experienced patients are very positive" commented **Wim Parys**, MD, vice president of clinical development at Tibotec. "TMC114 was selected for clinical development on the basis of its novel in vitro antiviral profile and potency against PI-resistant HIV."

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Federal HIV budget grows while states make big cuts

ADAP faces critical shortage, limits enrollment

The federal government's FY 2003 budget provides modest increases in HIV prevention and care funding, but that additional money won't meet drug treatment needs for the poor or offset significant cuts in state and city health budgets, experts say.

Congress increased funding for the Ryan White Comprehensive AIDS Resources Emergency Act by $96 million, bringing total spending under that bill to $2 billion. Nearly all the increase ($80 million) will go to the Ryan White AIDS Drug Assistance Program (ADAP) — about half of what AIDS organizations had requested.

The Centers for Disease Control and Prevention's HIV, STD and TB prevention budget also was increased by $34.7 million for a total of $1.2 billion. And the Minority HIV/AIDS Initiative was increased $25 million, for a total of $406 million. An additional $14 million was earmarked for the Housing Opportunities for People with AIDS program.

Although President Bush's budget for HIV care and treatment programs calls for a $100 million increase in ADAP, it assumes no increase in FY 2003 and delays the proposed increase until October, according to the San Francisco AIDS Foundation's HIV Advocacy Network.

At least 13 state ADAPs have already either limited access to antiretroviral treatments or closed enrollment to new clients. An additional seven states have reported the potential need to implement restrictions in early 2003 based on current funding levels and projected trends in program utilization, the Gay Mens' Health Crisis (GMHC) reports.

"Sadly, instead of confronting the issue head on, this President has chosen to tout illusory budget increases while actually cutting vital programs." says **Ana Oliveira**, executive director.

States facing difficult cutbacks

Faced with balanced-budget requirements and large declines in revenues, most states have had to cut health department programs. Massachusetts announced a $3 million cut in AIDS services, for example. The FY2003 funding cut combined with last year's budget cuts of $12 million to mean a 30% reduction in the state's HIV/AIDS program budget.

HIV care organizations say the reduced funding will interrupt care and support for even the most hard-core services, such as nutrition programs and home-care visits.

In California, Gov. Gray Davis's proposed 2004 budget has spared most AIDS treatment programs and includes $9 million in additional funding for ADAP. However, $7.2 million of that will come directly from the new copayments.

AIDS activists say the increase won't meet current needs and will require enrollment limits or

Highlights of federal FY 2003 HIV/AIDS budget

Federal spending for FY2003, which comes more than four months after the fiscal year began, totals $397 million. HIV/AIDS funding, both domestic and global, received modest funding increases. Here are the highlights, compiled by the San Francisco AIDS Foundation:

• ADAP received an $80 million increase. This was the largest increase for a domestic HIV/AIDS program.

• The Minority HIV/AIDS Initiative received a $25 million increase, growing to $412 million. The increases support the various agencies within the U.S. Department of Health and Human Services to enhance the access and quality of HIV services available through community-based minority organizations.

• The Housing Opportunities for People With AIDS program received a $14 million increase to $292 million. This represents the original request proposed by the Bush administration and is $58 million short of the program's request for FY 2003.

• Domestic HIV prevention efforts at the Centers for Disease Control and Prevention were increased by $5 million, to $701.6 million.

• Efforts to address the global AIDS pandemic were increased at the CDC by $39.2 million to $183 million and at the U.S. Agency for International Development (USAID) by $90 million to $630 million. Most of these increases, however, will support the Administration's Mother and Child Prevention Initiative.

• The U.S. contribution to the Global Fund in FY 03 will be $350 million, $150 million more than the President requested.

Source: San Francisco AIDS Foundation, HIV Advocacy Network.

removing drugs from the ADAP formulary. At the same time, Davis also has proposed cutting $1.25 million from HIV prevention efforts statewide and scaling back AIDS research at the University of California by $2.3 million.

Cities hit hard by AIDS, such as San Francisco and New York, face bigger problems. San Francisco's budget crisis, exacerbated by the Internet technology bust and tourism declines, could result in up to 300 staff reductions at the city's health department.

The head of the city's health department, **Mitch Katz**, MD, presented an initial cut of $37.5 million now and another $28 million later if necessary. Reductions would include funds for the AIDS hotline and HIV/AIDS support groups.

"These cuts are painful, and they're occurring in areas where there are currently unmet needs," Katz told reporters.

In cities across Texas, cuts have resulted in protests not seen in years. AIDS activists rallied this fall at the state capital to fight against the kind of cuts seen in San Marcos, where Community Action Inc., which received $66,000 in state funds in 2002, will receive no funds this year. Local health officials are calling for changes to ensure resources are funneled to areas with the highest rates of infection, such as Dallas and Houston. ■

Committee merger heralds integration of approaches

'This merger puts the best of both worlds together'

After more than 15 years of meeting separately, the two committees that advise the U.S. Department of Health and Human Services (HHS) on HIV prevention and care have merged into a single committee, HHS Secretary **Tommy Thompson** announced recently.

"This merger puts the best of both worlds — prevention and treatment — together for the benefit of all who are affected by this illness," he said.

The Centers for Disease Control and Prevention's Advisory Committee for HIV and STD Prevention (ACHSP) has met in Atlanta since the late 1980s. During the past two years, it has held several joint meeting with the Health Resources and Services Administration's (HRSA) AIDS Advisory Committee to increase efforts at integrating prevention and care.

The announcement that the committees would merge and meet alternately in Atlanta and Washington took committee members by surprise. However, most of them supported the move, seeing it as a significant and long-overdue

step toward filling the gap in the care-to-prevention continuum.

The merger is part of a national effort to improve both HIV and STD prevention in persons already infected with HIV. The CDC and HRSA are already working with the Infectious Diseases Society of America to develop prevention guidelines for providers who care for HIV-positive patients. A set of practical recommendations for integrating risk assessment, STD screening, and brief HIV prevention messages will be published this spring.

Divisions grew out of historical differences

The separation between the two committees reflects the historical differences that have partitioned HIV treatment and prevention. While the merger has been positioned as a win-win effort to integrate prevention and care, advisors from both committees voiced concern that the combined committee would diminish the role of the advisors.

ACHSP members were particularly concerned that prevention issues would get short shrift, considering that the budget for HIV care is many times larger than that for prevention.

"I hope that combining the two committees will not prevent us from having the kind of interaction and deep detailed knowledge of the programs of these two agencies that we need," says Jessie Milan, chair of the HRSA committee.

"I would like to think there is an increasing commitment to continue the merging of cultures that has already started," responds **David Fleming**, the CDC's deputy director for science. "This is just one more good reason to make it happen in fact."

HRSA administrator **Elizabeth Duke**, PhD, agrees, saying the merger will provide a richer staff collaboration. "Organizational culture is something that is valuable and something we encourage," she explains. "But by working together, we have an opportunity to do a lot more together than by alone. Having a natural marriage of interests and commitment is a positive thing for all of us."

Another concern is that the combined committee will be larger and also will only meet twice a year, whereas each committee had met three to four times a year separately.

"The full domain of the scope of the existing committees will be in this single unified committee," Fleming says. "So we are not eliminating individuals or the domain. We really are seeking instead to create an atmosphere that allows for a more integrated approach. I'm excited because being able to incorporate STDs into that mix of treatment and prevention, such as current activities with syphilis, will be a major step forward for our agency and for our ability to collaborate with HRSA."

"It will allow us all to be much more efficient and much more innovative," adds Duke.

There needs to be some thought of how to ensure that prevention is not overlooked, says **Cornelius Baker**, MD, executive director of the Whitman Walker Clinic in Washington, DC. "I want to make sure prevention doesn't get the shorter stick if the sticks aren't equal. It's easier and less politically volatile to talk about a lot of the care issues; the prevention issues have been difficult over the last year."

"This is a work in progress, and we will continue to evaluate and modify and learn from it," Fleming says.

Another downside of the merger is that prevention may become too focused on HIV-positives, says ACHSP member **Neil Schram**, MD. "I think it will be very difficult in this setting to focus on broad and narrow strategies for people who are HIV-negative," he says.

"There is uniform agreement in the department, both from HRSA and CDC, that we make sure we address the eclectic prevention messages to those who are at risk for HIV," Fleming responds. ■

Experts want CDC to hasten STD/HIV integration efforts

Recommendations include better guidance, models

As the Infectious Diseases Society of America prepares publication of guidelines for integrating HIV and STD prevention into HIV care settings, health officials are also pushing for better integration between STD and HIV prevention practices.

To that end, the Centers for Disease Control and Prevention's Advisory Committee on HIV and STD Prevention created a working group that has developed several recommendations.

The working group's overall conclusion is that programs need better leadership and models to

Taking steps toward STD/HIV integration

The National Alliance of State and Territorial AIDS Directors and the National Coalition of STD Directors have published a report on STD/HIV integration that provides reasons for integration as well as steps that state and local jurisdictions can take to support integration.

The reasons include:

- The same sexual behaviors that cause STDs also cause HIV. Prevention of HIV will benefit STD prevention, and prevention of STDs will benefit HIV prevention.
- Recent studies have demonstrated that being infected with an STD may make it 2 to 23 times easier to transmit HIV, depending on the specific STD.
- Many individuals infected with syphilis are also co-infected with HIV; nationwide, approximately 50% of men who have sex with men that have been diagnosed with syphilis were also HIV-positive.
- By identifying those patients in clinics who are infected with both HIV and other STDs and then treating their STDs, we may be able to reduce new HIV infections by as much as 27%.
- Because new HIV treatments have lessened the fear of becoming infected, behavioral interventions for HIV need to be augmented with biomedical interventions such as enhanced STD screening and treatment.

Steps for integration include:

- Develop integrated surveillance systems, data collection, software, and analytic approaches for tracking and evaluation.
- Develop behavioral surveillance and valid surveys and measures to address both HIV and STD issues (for example, behavioral and environmental factors).
- Integrate surveillance activities to include case-based, venue-based and population-based systems, as well as to include disease, behaviors, and social factors.
- Develop and disseminate STD screening and treatment guidelines to HIV and substance abuse providers to ensure familiarity and improve their ability to respond to patient concerns.
- Consider developing STD advisory groups, in coordination with HIV community planning, to focus on prevention priorities and clinical treatment guidelines.
- Cross-train STD/HIV staff in partner assistance and other services to help maximize resources and efficiency.
- Integrate STD, HIV, and healthy sexuality curricula in schools.

Source: National Association of State and Territorial AIDS Directors, 2002. ■

help clinics get beyond institutional and cultural barriers that have made integration slow and uneven.

The recent syphilis outbreaks in men who have sex with men, many of whom are HIV-positive, has underscored the need for better coordination of prevention services.

Top-level personnel changes at the CDC's Division of HIV Prevention and its Division of STD Prevention also make this an opportune time to make changes, say officials at the National Association of State and Territorial AIDS Directors (NASTAD).

This summer, NASTAD teamed up with the National Coalition of STD Directors to publish the report, "STD/HIV Prevention Integration." Among their recommendations is a call to federal agencies to "better articulate their goals and coordinate their efforts relating to funding for HIV prevention, STD prevention and treatment, HIV care and treatment, and substance abuse prevention and treatment." **(See other recommendations in box above.)**

Although integration has been pushed at the CDC for nearly five years, progress has been hindered by separate funding streams and fears of merging departments. Attitudes are changing, but more guidance is needed, the CDC work group noted.

"People are at the stage now that they know we should be doing more, but the question is what should we be doing and how much more, especially when we are challenged by funding sources and levels," says **Gail Bolan**, MD, director of California's STD control program and a co-leader in the workgroup. "Also, many programs don't know how to frame the issue. Are we talking about money, staff, messages, or planning? Integration means different things to different people."

After meeting over the past year, the workgroup came up with four recommendations for the CDC to consider:

1. The agency should hold a consultancy to discuss issues pertinent to the integration of HIV and STD prevention. Ideally, the meeting would be held jointly with the Health Resources and Services Administration, which oversees HIV care in the country. The meeting would address best practices and recommendations for removing barriers in both care and prevention.

A meeting report would provide programs and providers recommendations for integration of services for CDC and other funding agencies in making necessary structural changes.

As an alternative to the consultancy, the workgroup proposed a less comprehensive "briefing book" to provide background materials.

As part of the briefing, the CDC would interview STD and HIV program directors as well as the chairpersons of community planning groups to identify successes and failures with integration.

2. The CDC's National Center for HIV, STD, and TB Prevention would designate a staff person in the Office of the Director to serve as point person to coordinate ongoing issues in integration. This position is seen as increasingly important as STDs and HIV re-emerge in men who have sex with men.

3. The CDC should review existing and planned HIV initiatives, guidelines, and program announcements to ensure integration issues are included.

4. Mechanisms should be established to support regular meetings between HIV and STD prevention program staff at the project level to enhance ongoing communication and planning.

While removing funding restraints is seen as critical to increasing integration, there was agreement that the programs need to remain separately funded.

CE/CME *directions*

To complete the post-test for *AIDS Alert*, study the questions and determine the appropriate answers. After you have completed the exam, check the answers **on p. 52**. If any of your answers are incorrect re-read the article to verify the correct answer. At the end of each six-month semester you will receive an evaluation form to complete and return to receive your credits.

CE/CME *questions*

13. Which is NOT a reason that more HIV patients on antiretroviral therapy are having heart attacks?
    A. Better therapy is allowing patients to live longer.
    B. HIV-positive patients often have other risk factors for heart attacks.
    C. Protease inhibitors are increasing cholesterol levels.
    D. Antiretroviral drugs weaken the heart.

14. What was the unexpected outcome of the VaxGen AIDS vaccine trial recently completed in the United States?
    A. Only half the participants completed the trial.
    B. The vaccine had significant side effects, including severe rash.
    C. The vaccine provided more protection among blacks and Asians than among whites.
    D. Participants engaged in more risky behavior because they thought they were protected by the vaccine.

15. Which is the most important local factor in determining the cost-effectiveness of HIV interventions?
    A. How much money is spent on education
    B. HIV prevalence
    C. Where the intervention takes place
    D. The age of the targeted population, with older participants costing more money to reach

16. Which is NOT a reason why STD treatment and control is an effective HIV prevention strategy?
    A. Co-infection with an STD makes it easier for HIV to be transmitted.
    B. Rates of STDs, particularly chlamydia and gonorrhea, are at an all-time low and can be eliminated with extra efforts.
    C. Many individuals infected with syphilis are also co-infected with HIV.
    D. The same sexual behaviors that cause STDs also cause HIV.

"No one is interested in putting HIV and STD funding together. Everyone is clear about that," says **Dorothy Mann**, director of the Southeast Pennsylvania Family Planning Council in Philadelphia.

Opportunities for integration identified by the workgroup include: using STD data to target and evaluate HIV prevention activities; integrating STD and HIV prevention messages; and offering STD screening in HIV care settings and vice versa.

An example of the latter can be found in California, where syphilis elimination money is funding efforts at community-based HIV prevention programs to add STD screening and prevention messages, Bolan says. "At the same time, we hope to learn from them how we can do a better job of integrating HIV prevention and behavioral models, which is something STD programs have not embraced as quickly."

A critical issue raised by CDC advisors is the fact that some federal programs, such as Medicaid, don't reimburse for STD or HIV screening.

"The real key to making things happen would require providers to get paid for risk screening," says **Thomas Liberti**, MD, chief of Florida's Bureau of HIV Services. ■

CE/CME *answers*

Here are the correct answers to this month's CME/CE questions.

13. D — Antiretroviral drugs weaken the heart.

14. C — The vaccine provided more protection among blacks and Asians than among whites.

15. B — HIV prevalence

16. B — Rates of STDS, particularly chlamydia and gonorrhea, are at an all-time low and can be eliminated with extra efforts.

CE objectives

After reading this issue of *AIDS Alert*, CE participants should be able to:

- identify the particular clinical, legal, or scientific issues related to AIDS patient care;
- describe how those issues affect nurses, physicians, hospitals, clinics, or the health care industry in general;
- cite practical solutions to the problems associated with those issues, based on overall expert guidelines from the Centers for Disease Control and Prevention or other authorities and/or based on independent recommendations from specific clinicians at individual institutions. ■