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Acceptability studies have important role in microbicide clinical trials

Researchers also look to improve female condom use

Although obstacles remain before any one of the five microbicides in Phase III clinical trials are approved by the FDA, public health officials are grateful that at least one challenge has already been addressed, and that is the acceptability of the products.

Acceptability studies are fully integrated into the microbicide study process, even as investigators design and initiate research into finding a microbicide that will prove efficacious against HIV infection.

Research demonstrates a need for microbicides among women, particularly in the developing world. The Global Campaign for Microbicides of Washington, DC, has developed predictions of sales potential that indicate that a third-generation microbicide could have international sales figures that are nearly as high as the sales of male condoms.

Studying acceptability of the new product has been crucial to its development, experts say.

"One of our goals is to bring the behavioral side into the pre-development clinical pipeline, so we have acceptability very early in the pipeline," says **Jim A. Turpin**, PhD, microbiologist with NIH's National Institute of Allergies and Infectious Diseases (NIAID). He also is part of the Prevention Sciences Branch and the Topical Microbicide Group, both of NIH.

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COMING IN FUTURE ISSUES

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Editorial Questions

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Turpin and other NIH scientists discussed at the recent HIV Prevention Conference the behavioral and social data regarding acceptability of microbicides and how these can be integrated very early in the microbicide development process. Sponsored by the CDC, the 2005 HIV Prevention Conference was held June 13-17, 2005, in Atlanta.

"If you look across the board, you will find almost all clinical trials, whether for vaccines or microbicide treatments, have something about acceptability of the treatment," Turpin says.

Turpin says he's optimistic about the eventual commercial use of an HIV microbicide since there are five microbicides in Phase III or efficacy trials, ready to determine the major obstacle of proof of concept for efficacy.

"I'm very optimistic that if we have that many in, we'll have a broad assessment of a microbicide that's efficacious and what conditions under which it will be efficacious," Turpin says. "The other part that makes me optimistic is that for microbicides there is a robust pipeline, a broad base of compounds advanced and a broad base even further back in the development pipeline."

A drawback to microbicides is that it will likely be a few years before one makes it to the market, and even then researchers expect that the first microbicides to be approved by the FDA will be far less effective at preventing HIV than either the male or female condom, says **Theresa Exner**, PhD, research scientist with the HIV Center for Clinical and Behavioral Studies and an assistant professor of medical psychology, department of psychiatry, at Columbia University in New York City.

"The best guess is that early microbicides may only be about 60% effective," she says.

Nonetheless, public health officials and researchers are very enthusiastic about the prospect of microbicides being used for HIV prevention, Exner says.

"Everyone I talk to is very enthused conceptually about the idea of a product that is lubricant in format," she says.

Also, some public health officials argue that if the HIV prevention arsenal includes a product that is less effective, but more widely used, then it will increase the overall protection of the population, says **Susie Hoffman**, DrPH, research scientist for the HIV Center for Clinical and Behavioral Studies and assistant professor of clinical epidemiology at the Mailman School of Public Health in New York City.

"It can increase the overall level of population protection if more people are using it who have never used anything," Hoffman explains. "So even if the product has lower efficacy than condoms, if it has a high acceptability, and if people who were not using condoms begin to use it then the overall protection for a population can be increased."

The biggest challenge facing microbicide research is reaching the goal of proof of concept, Turpin says.

"And what will that be — a 100% efficacious microbicide, 80% or 50%?" he says. "That incorporates not only basic science, but also applied sciences, formulations, manufacturing, and social and behavioral sciences of whether it's acceptable, and if it is, how do we make it more acceptable."

Another challenge is convincing a major pharmaceutical company to buy in to the microbicide business, Turpin notes.

So far most of the money spent on microbicide research has come from NIH, other government entities, and nonprofit organizations, he says.

"We are actively through our initiatives and grant programs trying to fund and bring the big pharma into the microbicide business," Turpin says. "So we are providing through multiple programs money for basic research and pipeline development."

Case in point

Meantime, some scientists are frustrated by the lack of interest among the world media, health officials, and the public for the very effective and readily available female condom.

When it first came on the market, it was derided in media reports, and now it is never mentioned, Exner notes.

"The female condom provides an option beyond the male condom, and the marginalization of this method — people acting like it doesn't exist — is extremely frustrating when it's so badly needed," Exner explains.

The lack of popularity and acceptance for the female condom could be a good example of what happens when acceptability studies aren't incorporated into clinical research early on in the development of a prevention method.

"Acceptability of the female condom is an issue that was explored in more depth only after its development," Exner says. "So when this method was introduced it wasn't really carefully introduced with an eye toward acceptance by health care providers, and then the word of mouth and the press have been quite poor."

Exner and Hoffman were involved in research

about health care providers' perceptions of the female condom, and they, along with colleagues, discovered there were enormous prejudices against the method, based on word-of-mouth reports and not based on direct experience.[1]

"It's a method that's gotten a really bad rap, and it's one that I think is constraining what providers do when they're counseling on issues of use," they say.

For example, a study about the acceptability of the female condom among New York City health care providers found that they were skeptical about the condom's contraceptive efficacy, with only a little more than one-third of the providers reporting they would recommend the female condom as a primary contraceptive.[2]

South African providers were concerned about the female condom's appearance and its affects on sexual pleasure.[2]

Another reason the female condom has not caught on internationally is because of its cost and structural issues, such as too few national programs promoting its use and the lack of provider training to introduce the female condom to women, Hoffman says.

Its benefits are many, Exner notes. First, it provides women with a way to protect themselves, rather than convincing or relying on their male partners to wear a condom, she says. Secondly, studies have shown the female condom offers a more pleasurable sexual experience than the male condom.[3,4]

"The female condom doesn't require a man's penis to be erect, and a woman can put it in before sex, and it can stay in her as long as she likes before sex," Hoffman says. "Polyurethane, which is what it's made of, transmits heat better than latex, and it doesn't cause allergies."

The transmission of heat has been reported by women who use the condom as being quite important, and the female condom presents less of a barrier between bodies than does the male condom, Hoffman adds.

Drawbacks to the female condom are similar to those of any barrier method of birth control, which mainly is that people are not as fond of these devices. Also, the female condom costs about nine to 10 times more than the male condom in developing nations, even in places where the World Health Organization (WHO) and others are distributing them at a reduced cost, Hoffman notes.

In the United States, the female condom costs around $3.50, but some Medicaid programs are offering reimbursements for its use, Exner reports.

"One of the biggest indications that the female condom is not even penetrating the consciousness of people working with women is in the year 2002 there were only 500 Medicaid reimbursements in the entire year for New York state," she says. "That's enough prevention for about four people, so that speaks to the need for education to consumers about the condom's availability for reimbursement."

Also, although WHO has not yet endorsed the reuse of female condoms, there is ample evidence that these can be reused a number of times, Exner says. "They've basically tortured female condoms washing them in bleach and all kinds of substances, and they're incredibly hardy."

Prevention scientists have addressed the issue of improving the use and acceptability of the female condom through training of health care workers, Hoffman says.

"Many health care workers believe it's not a good method for women to use because it doesn't protect against pregnancy — but this is inaccurate," she says. "It does protect against pregnancy better than diaphragms."

In South Africa, where the female condom program was integrated into all family planning settings, the use of the female condom has increased, Hoffman reports.

While there have not been clinical trials to prove the female condom's HIV prevention efficacy, it has been proven highly efficacious against infection by sexually transmitted diseases, Exner says. "And while people are talking about an undeveloped microbicide, the female condom is here, and there is considerable evidence that the availability of this method is an important part of the methods that can empower women to negotiate with their partners in new ways," she says. "And it provides an option beyond the male condom."

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Epidemic is shifting to blacks, Hispanics

Most common transmission is MSM

The most recent data from the CDC estimate that about one-quarter of the more than 1 million people living with HIV/AIDS do not know they are infected.

The data also show rising diagnoses among men who have sex with men (MSM), particularly those who are African American and Hispanic.

Although the data from 2003 are based on information from only 30 states, not including New York and California, this estimate provides the clearest picture to date of the impact of the epidemic on the American population.

"What we do is use information on new HIV diagnoses and data on the stage of disease when a person was diagnosed," says **Kate Glynn**, DVM, MPVM, an epidemiologist with the division of HIV/AIDS prevention at the CDC.

CDC officials estimate between 1.04 million and 1.19 million Americans are infected with HIV, and 24% to 27% of them do not know they are infected, she notes. "Knowing what we do about AIDS diagnoses in a balance of areas, exposure category, we extrapolate a distribution in those subgroups," Glynn says. "So we have estimates for all groups for the entire U.S."

The surveillance data also shows the greatest impact of the epidemic is among African Americans and Hispanics, she points out.

Investigators determined that 47% of people living with HIV/AIDS are African American, 34% are white, and 17% are Hispanic, and 74% are male, Glynn says.

The most common transmission group remains MSM (45%), while heterosexual contact accounted for 27%, and injection drug use accounted for 22%, Glynn says.

Among MSM, HIV diagnosis rates, between 2000 and 2003, were 4.4 times higher among African American men and 2.1 times higher among Hispanic men than among white men.[1]

Epidemiologists ideally would determine the burden of the HIV epidemic on a particular population, but there are no estimates for the number of MSM or high-risk heterosexuals in the United States, Glynn says.

Investigators have looked at the burden of a particular transmission category among the general population.

The findings suggest the rate of HIV diagnoses associated with MSM sex increased in each ethnic group, while the rates of diagnoses among injection drug users had a slight decrease or were stable in all ethnic groups. The findings were similar for women, Glynn says.

"In every transmission category, the rates were the highest among African Americans and second highest among Hispanics," she reports. "So clearly in terms of implications for prevention, this should remain a high priority in every racial ethnic group among men, and prevention of transmission should remain a high priority among women, especially black women."

CDC investigators also have examined the pool of infected people to see if there is something that could indicate whether these findings would change in the future, Glynn reports.

"We compared those among the diagnosis cases as compared with those living with AIDS, and what we saw is the cases of new HIV diagnoses were more likely to be female, black, and associated with high-risk heterosexual contact," she says. "This suggests this is more likely to be where the future is heading to some extent, with more diverse populations continuing to be impacted."

Although the CDC does not believe new diagnoses are identical to new infections, it is known that new HIV diagnoses are more likely to represent new infections than are new cases of AIDS, Glynn says.

The challenge is to reach the highest risk groups with tailored prevention services, she notes.

Another trend is that new HIV diagnoses among injection drug users are a little lower than those among AIDS cases, Glynn adds.

"That's consistent with surveillance data that suggest rates of new HIV diagnoses attributed to IDU are stable or decreasing," she says.

CDC officials also have found that patterns of HIV diagnoses among people, ages 13 to 24, confirm recent reports of a resurgence of HIV among young MSM.[2]

The number of diagnoses among adolescent and young adult men rose from 1,040 in 1999 to 1,471 in 2003, in 25 states.[2]

In the same age group, the new diagnoses among women have steadily declined from 1994 to 2003, Glynn says.

For young men, there initially was a 30% decline in new diagnoses between 1994 and 1998, and then there was a 41% increase between 1999 and 2003,

she says. "The recent increases among males were driven primarily by a 47% increase among young adults, ages 20 to 24, who are MSM, and the majority were black, non-Hispanics. It's important to remember that what are reported here are new HIV diagnoses, so it's not possible to determine whether the trends are due to increased HIV testing or a true increase in new HIV infections."

Some researchers have concluded that treatment optimism and a decreased fear of infection are playing a role, so they're calling for more intensive efforts at prevention directed toward young MSM to reverse the recent trends, she notes.

"I think it's also important to continue treatment among females and young adults to sustain recent declines," Glynn adds.

"More persons are living with HIV than ever before, and what we know is treatment successes have brought new challenges," she says. "It's clear that effective treatment is a godsend for HIV-positive individuals and allows them to live longer and healthier lives, but it also means there's a growing population in need of services, and increased prevalence means an increased opportunity for HIV transmission."

There also is a challenge of helping high-risk and HIV-infected people maintain safe behaviors over a lifetime and not just during crisis times, Glynn adds.

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Non-HIV-related deaths rises to 26% in NYC

IDUs had highest mortality rate

New research hammers home the point that HIV providers need to attend to their patients' overall health needs and not just to HIV-related morbidity.

"They need to have more of a primary care model in mind that manages all aspects of people's health," says **Judith Sackoff**, PhD, director of HIV/AIDS surveillance for the New York City Department of Health and Mental Hygiene.

Sackoff co-authored a study that found mortality among New York City residents, ages 13 and older, who were diagnosed with AIDS, rose to 26% of all deaths among this population in 2003. By comparison, only 7% of all deaths among persons living with AIDS were for non-HIV causes in 1995.[1]

About 75% of non-HIV-related deaths among persons living with AIDS in New York City were related to cardiovascular disease, cancer, and substance abuse. Also, injection drug users were significantly more likely to die from non-HIV-related causes.[1]

"Even though we found that, in general, people with AIDS in New York were dying of non-related HIV conditions, including cardiovascular disease, diabetes, etc., substance use was a significant cause," Sackoff explains. "Substance use is not a leading cause of death among all New Yorkers, but it accounted for more than one-third of the non-HIV-related causes of AIDS, and it was consistent across groups of men, women, blacks, Hispanics, and whites."

The study analyzed data between 1999 and 2003, the period when highly active antiretroviral therapy (HAART) was widely adopted. Here are some of the findings for persons living with AIDS during that period of time[1]:

- the number of people age 50 or older increased from 2,904 to 16,900, almost sixfold;
- the AIDS population has a high rate of smoking and substance use;
- substance use (7.3%) was the leading cause of non-HIV-related deaths;
- major cardiovascular diseases accounted for 5.4% of all non-HIV-related deaths;
- malignant neoplasms accounted for 4.7% of all non-HIV-related deaths.

The population of people living with AIDS in 2003 included 70% men, 45% blacks, 33% Hispanics, and the median age was 45 years, Sackoff reports. "As people live longer due to antiretroviral therapy, they are at more risk for the kinds of things [those getting older] are at risk for," she notes. "So it's the graying of the population of people living with AIDS."

Investigators gathered data from death certificates that indicated that lung cancer was the leading cause related to cancers, followed by breast cancer in women and liver cancer in men, Sackoff notes. "What we reported is the underlying cause of

death. Every death certificate has multiple causes."

Trained specialists sorted through the multiple causes and following a set of guidelines identified the underlying cause of death, Sackoff adds.

"It's an exceedingly complex process, and we've learned an awful lot from this," she says.

The study was limited in what conclusions could be drawn from cause of death and treatment, Sackoff notes. "We wish we could take a look at cardiovascular disease related to antiretroviral therapy, but we can't look at that because we have no information on the treatment people were on before they died," she says. "And the way deaths are coded on certificates is not subtle enough to pick up cardiovascular disease related to HIV treatment, so we were unable to address that question."

However, investigators were able to classify a large number of conditions as substance use-related, including liver disease, hepatitis C, and overdoses, Sackoff says.

Likewise, researchers knew that other lifestyle habits among people living with AIDS had contributed to the non-HIV-related causes of death.

"We know there are very high rates of cigarette smoking among people with AIDS," Sackoff says. "About 50% of people with AIDS in New York City are smokers, compared with 22% overall; and there are high rates of alcohol use and substance use. These are the things that have become important causes of death to people with AIDS."

While AIDS continues to kill people, those living with the disease are going to have to face the fact that their own behaviors also are going to kill them, Sackoff says.

The study also found that while suicide is only ranked seventh in the causes of non-HIV-related deaths overall, it was the second leading non-HIV-related cause of death among men who have sex with men, Sackoff points out.

"That was something we had not seen reported before, and it's something that is obviously very much of concern," she says. "I think mental health issues in general are very important for people living with AIDS because they won't kill directly, but perhaps suicide and substance use are indirect manifestations of the disease."

One last important point made by the study is that people still are dying from AIDS, despite the huge advances made in treatment, Sackoff notes.

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AIDS Alert *Update: 21st Century Prevention Work*

(Editor's note: AIDS Alert *provides the second part in the series of stories based on how HIV prevention funding and interventions are focusing on evidence-based programs. In this issue are stories about the challenges in adaptation and the trials and tribulations of investigators working on adapting two different, evidence-based interventions.)*

Adapting behavioral interventions is complex

Myriad factors complicate process

HIV-prevention researchers describe many frustrations with the process of adapting community-based intervention work to fit into the mold of one of the available evidence-based HIV interventions.

Increasingly, states are awarding HIV prevention grants only to community-based organizations (CBOs) that base their prevention work on one of the dozen HIV interventions sanctioned by the CDC and included on the Diffusion of Effective Behavioral Interventions (DEBI) list. This has increased demand for strategies in adapting a local organization's resources, experience, and target population to fit a DEBI, experts say.

However, behavioral scientists say this adaptation is difficult to do well, even when there are ample resources. A variety of factors may impact the translation of an evidenced-based prevention program, but among these are important factors regarding the capacity of the organization that will be using the intervention, says **Bart Aoki**, PhD, associate director of the Universitywide AIDS Research Program, University of California, Office of the President, in Oakland. According to Aoki, these factors include the following:

- The strength and maturity of the service systems within a specific organization, including how long the CBO has existed and how strong the CBO is in terms of consistency of staffing and having procedures in place for delivering services.
- The overall climate for implementation of innovation within a particular community or organization, such as how open the organization

is to change and adopting new ideas, and what incentives and processes are in place to reinforce or support the change.

• The organizational capacity and fitness of an organization to reflect community values, because if what's developed fits within the values of an organization, it's more likely to be implemented.

Other problems with translating evidenced-based interventions is that researchers and public health policy-makers do not yet know how much an intervention may be tailored and still remain effective, Aoki says.

Are DEBIs really the future?

Some those working in the trenches of HIV prevention express skepticism that adaptation of DEBIs is the best way to achieve prevention results.

"The fact that DEBI models may have been tested successfully once or twice does not automatically make them the future of HIV prevention as we know it," says **Mark Bond-Webster**, an outreach worker at Perception Programs in Willimantic, CT. The 35-year-old CBO was one of the few in Connecticut to receive an increase in funding for the implementation of two DEBI programs this year.

"I have a real concern that agencies are going to be funded to do DEBIs without necessarily having the resources and skill sets to implement those DEBIs correctly, so what you're going to get are poorly-implemented DEBIs to replace the previously effective interventions," he says.

A CDC official acknowledges the challenges CBOs and researchers now face in adapting prevention programs to fit the DEBI list, but he says is to be expected during a transition period.

"When we're trying to build national capacity to move science into practice, we're in a catch-up game here," says **Charles Collins**, PhD, supervisor health scientist and science application team leader with the CDC.

He compares the move from what the work CBOs traditionally have done, which he says was mainly HIV prevention outreach intervention and handing out condoms, to evidence-based interventions, to the theory, described in the 1995 book *Diffusion of Innovations*, written by Everett Rogers.

Rogers had explained an experiment of trying to convince Western farmers to switch to a new type of corn that would produce better crops, Collins says.

After launching a big diffusion effort to educate farmers, researchers found that in the first year farmers had planted half their field with the new corn and half with the old corn, he explains.

"Now I think there's a very important message for HIV in that," Collins says. "The message is that CBOs have a role in protecting their communities, and they have a role in making sure these are culturally competent and effective interventions."

Still, in the first few years that they try the evidence-based interventions they will mix old prevention practices with the new prevention practices, just as the farmers mixed old seed corn with new seed corn, he adds.

"So when I hear a CBO is doing the Mpowerment intervention and they're only doing half of it, instead of thinking they're 50% noncompliant, I think it's better to think they are showing 50% trust in us, and they're willing to try it," Collins says.

Eventually, CBOs will master the new interventions, just as the farmers finally had switched entirely to the new corn, he notes.

However, even when CBOs more fully embrace evidence-based interventions, some significant challenges will remain in order for these to work in very different situations.

"The basic argument advanced is the kind of model that is dominant right now in disseminating prevention programs is problematic in multiple respects," says **Robin Lin Miller**, PhD, associate professor at Michigan State University in East Lansing.

"One way in which it's problematic is there is often a real mismatch between what gets designed and tested in these demonstrations and what communities have the capacity to implement," Miller says. "It's not just the issue of financial costs, there are a whole host of things that go into capacity of the organization to carry out a program, and I think we don't understand enough about that."

Also, there is a bias in the HIV prevention field that the evidence-based programs are better than what they might replace, and that hasn't been proven, Miller says.

"While it is the case that CBOs don't have evidence to support their practice, that isn't the same thing as saying their practice is of no benefit," Miller explains.

So while there is evidence the DEBIs have been reliable to produce a small effect, investigators have no idea how that effect would compare to a range of programs in a particular community with which they might be evaluated, Miller says.

"There are many cases where the DEBIs might be better, but also there might be cases where they might not be," Miller adds.

"The process of tailoring requires more study and guidance," Aoki says.

How much can be modified?

"Do you need to replicate an intervention with 100% accuracy or 80%?" asks Aoki. "What aspect of it must be retained to enable you to benefit from the innovation that's inherent in that particular program?"

An analysis of 50 projects showed that there were many factors that contributed to sound scientific interventions, he reports. "But one that seemed most prominent is whether there was a history of prior collaboration between community service organizations and evaluators and researchers," Aoki says. "So it looks like, and this is something we've been trying to encourage, is a culture of collaboration between academics and the community."

More money needed

The reality of HIV prevention work is that too little funding is available to develop these types of collaborations and careful tailoring, prevention researchers say.

Meantime, some states are stepping up the pressure for DEBI use, despite the challenges inherent in making these interventions work in populations for which they were not designed.

For example, one of the only DEBIs designed specifically to target a Latino population of men and women is the VOICES/VOCES intervention, which stands for Video Opportunities for Innovative Condom Education & Safer Sex.

It was designed to increase condom use among heterosexual African Americans and Latinos who visit sexually transmitted disease (STD) clinics. If a CBO decides to use this intervention for a population of heterosexual Mexican farm workers, who have very limited access to health care clinics and live in rural migrant camps, there may be a problem finding an appropriate video because the ones designed for the initial intervention are suited for an urban Latinos who can watch the video in an STD clinic, says **Scott Rhodes**, PhD, an assistant professor in the department of public health sciences at Wake Forest University School of Medicine in Winston Salem, NC.

"So we say we'll implement VOCES, but since we don't have an appropriate video, we'll come up with a skit, and all of a sudden the funders say, 'You're not doing a DEBI,'" he says. "But the CBO says, 'In these farm camps there is not good video access, and the videos developed are not appropriate, and we don't have the knowledge to develop a good video, but we can train three people to act it out at the camp site.'"

Although the CBO's goal to improve condom use is the same as the DEBI's goal, and although the same type of prevention message would be given out in the skits as would be in videos, the funding entity says that because a video wasn't used, there would be no funding for the intervention, Rhodes adds.

It's that type of hypothetical situation that has occurred in North Carolina and elsewhere as some states have created stringent and sometimes arbitrary criteria for what has to be included in DEBI adaptation, Rhodes and other researchers say.

"All of these DEBI interventions offer good empirical evidence that behavior can be changed, and we can do something useful, but they're not necessarily perfect for the communities we're working with," Rhodes says. "We are creating a standard, but I'm not sure we know whether the standard we're creating is the right standard and will be effective across the board." ■

A closer look at two popular interventions

Mpowerment and Street Smart being adapted

Some HIV prevention researchers are learning firsthand how challenging it is to translate existing evidence-based interventions for different populations and dissemination. Investigators are learning more about how to translate the Mpowerment project and Street Smart for use in communities and populations that are different from the interventions' original use.

They are discovering that some challenges can be predicted, but many are small nuances that become important as an intervention is changed. Their experiences suggest that it might be naïve of federal and state prevention funders to expect a community-based organization (CBO) to develop its own adjustments to an evidence-based intervention and still achieve effectiveness.

"I think there is merit in implementing programs that have been shown to be scientifically effective, but the idea of coming up with an idea and winging it and expecting that to be effective is ridiculous," says **Susan Kegeles**, PhD, a professor and co-director for the Center for AIDS Prevention Studies at the University of California-San Francisco.

"It's a huge challenge to ask CBOs without regard to some of the organization's characteristics to tailor and adapt on their own," says **George Ayala**, PsyD, director of the Institute for Gay Men's Health, David Geffen Center in Los Angeles. He is involved with a translation of Street Smart for use among young Latino men who have sex with men (MSM). Street Smart initially was designed to be used with runaway and homeless youth, ages 11 to 18.

Kegeles and co-investigators developed the Mpowerment project, which was designed as an intervention for MSM, including acculturated Latino men, ages 18-29 years. The intervention's strategy includes outreach, social marketing, discussion groups, and other methods for providing safe sex and risk reduction messages.

Both Mpowerment and Street Smart are on the Diffusion of Effective Behavioral Interventions (DEBI) list of 12 HIV prevention programs, selected as evidence-based intervention strategies by the CDC.

Mpowerment: Better training needed

• **Mpowerment:** Investigators had tested Mpowerment in communities of 60,000 to 120,000 people in Oregon, California, Texas, and New Mexico, Kegeles reports.

"As we got good results from our studies and published those results and made presentations, we were struck by the huge numbers of requests for our curriculum," Kegeles says. "We were so busy thinking about getting the project funded, having a randomized control trial, and dealing with the politics in each community that we hadn't thought about such things."

However, once the CDC provided a funding grant for developing curriculum or replication packages, the investigators applied, received funding, and went to work, she says.

"Our first attempt at a replication package was for young gay and bisexual men, but it was packaged for organizations," Kegeles says.

At first the translation efforts were informal: Mpowerment was put on the CDC DEBI list when the list was started in 2003, and when organizations called for information, investigators would send them the available materials, Kegeles says.

"We'd give it to a local organization and help them write grant proposals to get funding for it," she says. "So we would give the materials to the organization and do some brief training and hope that would work because it would emulate the real world."

But Kegeles and colleagues quickly recognized that it didn't work; they would need to provide technical assistance to CBOs, and they didn't know how to fund that service.

"We always describe it as an airplane that was going down a runway and never lifted off," she says. "We realized the manual had to be better, the training had to be better, and we had to have some exercises so people could see what the interventions felt like, and we needed to be involved and have ongoing technical assistance."

This realization led Kegeles and co-investigators to apply for a federal grant from the National Institute of Mental Health (NIMH) to translate the research into practice by developing the Mpowerment Project Technology Exchange System, which provides CBOs with technical assistance, training, web site information, and other materials.

Now the system is being tested with 70 organizations around the country.

So far all the results of this large translation project are anecdotal, but interesting issues have arisen, Kegeles says.

Some of the CBOs who have wanted to adapt the intervention for use among different age groups, and others want to use it for young women as well as young men, she says.

At least one organization called to ask about adapting the intervention for use with incarcerated women, which would be a major stretch, Kegeles says.

"We expressed our concern about that," she adds. "One aspect of the intervention is it's supposed to be implemented by young men for young men, and they are decision makers of the project. Some organizations' higher-ups have a hard time with that because they're concerned young men might make a terrible decision."

Watching CBOs make decisions about translating Mpowerment has been fascinating and aggravating, she notes.

"They're struggling right now with less money, and they're trying and are passionate about these issues," Kegeles says.

For example, when investigators ran the Mpowerment intervention it cost $130,000 a year, but some organizations might be trying to implement it with a budget of $15,000 per year, she reports.

Through the technology exchange program, investigators are learning more about how interventions work in the real world, including what's possible and what barriers exist, Kegeles says.

One challenge is adapting an intervention for different ethnic groups, particularly when all of the original researchers are white. "So what I've been trying to do is bring people of color onto my research team," she explains. "And I make sure I work with communities closely to make up for the fact that I'm not black."

In working with black CBOs, investigators learned that the terms MSM, gay, and bisexual are not the words black MSM use to describe themselves, Kegeles notes.

"The other term is same gender loving (SGL), and it's becoming an acceptable term in Los Angeles," she explains. "Gay is white middle class and effeminate, and SGL is just men who are attracted to other men regardless of whether they'd call themselves gay or bi or straight."

Through boards of cultural experts and focus groups, researchers learn what is missing and what needs to be addressed in their intervention.

"We needed to get into issues about internalized homophobia and internalized racism," Kegeles says. "We have not finished developing the revised Mpowerment project, but this is an issue we know we have to get into."

The cultural experts and focus groups indicated that there are many other issues that need to be addressed before Mpowerment can be translated for a black population, including helping participants deal with life skills, including finding homes and jobs, she says.

"You have to do more because the complexities of life for young black men are just so much greater," Kegeles says.

While Kegeles and colleagues would like to further develop the program and assess its efficacy, but finding funding in these tight budgetary times will be difficult, she says.

At the very least, investigators might be able to provide a criteria list for how Mpowerment should be used by CBOs, Kegeles says.

"We're hoping at the end of the project we can say, 'These kinds of organizations make sense to implement these interventions under these kinds of conditions, but under these other conditions it doesn't make sense,'" she says.

Street Smart: Making it age appropriate

• **Street Smart:** With funding from the University of California and the state of California, Ayala and colleagues have been studying the translation process involving the Street Smart intervention.

"One thing we liked about Street Smart was it was adapted once before for use with gay youth in New York City," he says.

First, researchers convened a core group of health educators and facilitators to review the original Street Smart curriculum, and then they

CE/CME *questions*

5. Research through mid-2005 has shown that the first microbicides to achieve proof of concept were how efficacious?
   A. 100%
   B. 80%
   C. 50%
   D. Proof of concept had not yet been achieved

6. The most recent CDC data suggest that what percentage range of Americans infected with HIV are unaware of their infection status?
   A. 15%-19%
   B. 21%-25%
   C. 24%-27%
   D. 33%-37%

7. New York City public health data for 1999-2003 show that the number of people age 50 or older has increased by approximately what amount?
   A. Three times
   B. Four times
   C. Five times
   D. Six times

8. The world's fastest growing HIV epidemic, according to data from 2002 to 2004, is in what area of the world?
   A. East Asia
   B. Sub-Saharan Africa
   C. The Caribbean
   D. Eastern Europe

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. 96**. 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.

met with focus groups of young Latino MSM, who would be the target population, Ayala explains.

"The core group decided to rename it "Life Smart" or Nuestras Vidas, and that adaptation process took about 12 months to do," he says.

As researchers conducted in-depth interviews with facilitators and staff, they found that young Latino MSM wanted more experiential education, while the staff said they needed more didactic approaches, Ayala notes.

Also, health educators wanted researchers to incorporate into Life Smart some of the features of another intervention called Hermanos de Luna y Sol, which had been created a decade earlier but was not an evidence-based intervention. Because it was not part of the DEBI list, researchers had to decline the suggestion, he says.

You need more than one

Some of the nuances of Street Smart that needed to be changed as it was translated into Life Smart, included the way the original intervention had facilitators help participants identify their feelings. The original program had facilitators put up a large picture of a thermometer on the wall, numbered from zero to 100, where 100 represented very anxious, very sad, or very angry feelings. Since Life Smart was being adapted for the age group of 18-24, instead of the Street Smart's 11-18 population, it was decided that type of tool would not work, Ayala says.

"The group wisely wanted to have a pedagogical approach that was more age appropriate, but didn't lose the importance of the discussion of affect in the context of problem-solving," he explains.

Another minor change was reducing the 10 sessions to eight because the educators and participants said the target population wouldn't sit for the 10-session intervention, Ayala adds.

The translation study ended in June, and data still are being analyzed, Ayala says.

Researchers have observed that organizations that had an easier time integrating the intervention were those who had a broader prevention program already in place, Ayala says.

"The intervention when integrated represented a complement to those rather than a free-standing intervention, and that's a very important finding," Ayala notes. "They work better when they are a part of a complement of programs." ■

CE/CME 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. ■

CE/CME *answers*

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

5. D; 6. C; 7. D; 8. A.

AIDS ALERT®
INTERNATIONAL

UNAIDS report focuses on Asia and cites growing epidemic in the East, particularly China, Indonesia, Vietnam

HIV has spread to all 31 China provinces

The world's fastest growing HIV epidemic now is in East Asia where the virus is rapidly spreading in China, Indonesia, and Vietnam, international health officials say.

"In East Asia, the number of new infections increased from 120,000 in 2002 to 290,000 in 2004," says **Swarup Sarkar**, MBBS, MD, MS, programme development advisor for the UNAIDS Regional Support Team, Asia and Pacific, headquartered in Bangkok, Thailand.

While this increase is not worse than predicted, it does show that the epidemic is now taking off in the region, and it is a greater increase than what is seen in Eastern Europe and Africa, he points out.

"In the same period, Eastern Europe and Central Asia recorded 210,000 new infections in 2004, compared with 190,000 in 2002," Sarkar notes.

Also, sub-Saharan Africa's new infection rate was 3.1 million in 2004 vs. 2.9 million in 2002, he says.

The epidemic's current growth in Asia will result in an additional 12 million people infected with HIV in Asia and the Pacific within the next five years, says **J.V.R. Prasada Rao**, MSC, director of UNAIDS Regional Support Team, Asia and Pacific, who spoke about the epidemic in July at the Seventh International Council on AIDS in Asia and the Pacific (ICAAP), held in Kobe, Japan.

With a rapid scaling up of HIV prevention and care programs, at least half of these infections could be prevented, Rao says.

Drugs, sex contributing factors

A variety of factors have contributed to the epidemic's rise, according to a recent UNAIDS report.[1]

Population mobility is associated with increased vulnerability to HIV infection; and in Asia, an estimated 5% to 10% of the population moves within each five-year period.

Mobile workers are more vulnerable, with domestic workers sometimes at risk of sexual coercion and workers who travel routinely at risk due to more frequent contact with sex workers.

In China, where HIV has spread to all 31 provinces, much of the spread of the epidemic is due to injecting drug use and paid sex with the country's dramatic economic changes and new migratory patterns as additional factors, UNAIDS officials say.

"Contributing factors to rising infection rates in China are known to be those associated with transitional economies, rapid growth of the economy, fast growing incomes, population movement, and a changing of social values towards commercialization and entertainment, etc.," Sarkar says.

Also, despite the well-known harm reduction methods for preventing HIV infection through injection drug use (IDU), such as needle exchange programs, these prevention programs have not played a significant role in combating the Asian HIV epidemic, he adds.

"In spite of known evidence on harm reduction, it requires a change in policy, decriminalization, detailed operational plans, and human and financial resources," Sarkar explains. "As a result, the overall coverage for harm reduction programs aimed at injection drug users has remained at only 5% in the region."

There are 3 million injection drug users in Asia, and all countries in the region now report IDU problems, he says.

UNAIDS data show that in some Indian cities, the epidemic's spread through the IDU community

has been brutally rapid: In Chennai, for instance, 26% of drug injectors were infected with HIV when a sentinel site was started in 2000, but by 2003, 64% were infected.

Also in Jakarta, Indonesia, one-half of injection drug users test positive, and more than 70% of IDUs test positive in Pontianak, Indonesia, according to UNAIDS data.

"Injecting drug use is widespread throughout the region, and introduction of HIV into drug user networks can mean a rapid spread of the virus into the general population, through sex with partners or commercial sex work to pay for drugs," Rao says.

"HIV has been reported in almost all countries reporting IDU problems with the exception of Laos and Cambodia," Sarkar says. "Out of 13 countries surveyed, only seven have IDU policies, and only three had an operational plan to support the policy."

As a result, the overall resources for IDUs are less than 10% of what is required, Sarkar says.

Despite taboos and social constraints, HIV prevention work and resources should be concentrated to impact the vulnerable populations of injection drug users and sex workers, Rao points out.

"ICAAP provided a focus for harm reduction, which — as we all know — has faced major scrutiny in the past few months, with battles raging around terminology and morality," he says. "There is now consensus on harm reduction in Asia and the challenge will lie in scaling up."

Government efforts critical

It can be done with governmental backing. For example, in Malaysia, needle exchange is government policy, despite strong religious opposition, Rao says.

International financial assistance for HIV prevention and care in Asia has been increasing, with an estimated rise from just under $700 million in 2003 to an expected $1.6 billion in 2007.[1]

However, Asian governments and communities will need to provide strong leadership in order to present the epidemic from becoming a disaster, Rao says.

"AIDS responses must be anchored in the community and owned by the community if they are to work in the long term," Rao says. "Without the participation of civil society and of those most directly affected by the epidemic, responses will not work."

For instance, in China, Indonesia, and Vietnam, where the epidemic is growing among the fastest in Asia, the three countries have demonstrated increased political commitment at the very top level, Sarkar says.

"In all three countries resources have increased to almost double during the last two years," he says. "These countries have taken steps towards decriminalization of the most vulnerable populations, including IDUs, and, in some countries, for sex workers and men who have sex with men."

In China, the government has taken decisive action, and progress has been made in HIV prevention and treatment, including these measures, Sarkar says:

- methadone treatment programs for drug users;
- adoption and implementation of provincial policies, including condom promotion;
- calls for greater involvement of nongovernmental organizations and private sector companies in the fight against AIDS.

"The China Cares Project, with the help of the Global Fund to Fight AIDS, TB, and Malaria, managed to get 15,000 people on antiretroviral treatment by May 2005," Sarkar says.

In Vietnam, the government declared 2005 as the "Year of HIV Implementation," and provided a 75% increase in national spending on AIDS programs, plus receiving more than five times the international assistance between 2003 and 2006.[1]

And the Viet Nam Women's Union, which has 12 million members, is leading national efforts to reduce HIV stigma and discrimination while improving HIV education among women and girls.

Also, Cambodia and Bangladesh have demonstrated political commitment and strong policy to supporting prevention programs for sex workers and IDUs, Sarkar reports.

UNAIDS data show that Bangladesh has reduced the spread of HIV among sex workers and other vulnerable groups through HIV prevention interventions. While it was entirely likely HIV prevalence among sex workers would have been as high as 10%, it's current level is 1%, UNAIDS officials say.

And Cambodia has joined China, India, and Indonesia to dramatically expanding access to HIV treatment, according to UNAIDS information.

While these improvements provide a reason for optimism, work still needs to be done to prevent millions more HIV infections, officials say.

This will require even countries with low prevalence rates, including Bangladesh, Japan, and the Philippines, to commit to HIV prevention programs and funding, Sarkar says.

"All these countries can prevent the spread of the epidemic by early intervention, saturation of prevention programs for vulnerable communities and young people, political commitment, and increased or continued funding on HIV prevention programs," Sarkar says. "HIV is increasing in Japan among MSM and IDU communities, but the policies and programs have not been developed to reflect this increase."

It also will be a challenge for countries such as Thailand to prevent AIDS complacency from taking hold and resulting in a rebound of the epidemic.

"Success factors and a consequent slipping in prevention programs have been seen in the U.S. and in many European countries where more emphasis has been put on care," Sarkar explains. "The solution lies in continued prevention efforts both by governments and civil society, monitoring the changing dynamics of the epidemic and adjusting the response accordingly."

Meantime, the international community should continuously monitor and discuss the HIV epidemic at all high political forums, including G-8 summits, he suggests.

Reference

1. A scaled-up response to AIDS in Asia and the Pacific. Produced by UNAIDS and UNAIDS Regional Support Team for Asia and the Pacific, Bangkok, Thailand. June 2005; 1-40. Web: www.unaids.org. ■

About 1 million people in developing countries now receive HIV medications

Achievement falls short of WHO's '3 by 5'

The world's health community has succeeded in bringing antiretroviral treatment to about 1 million HIV-infected people in developing nations, which highlights both the progress made and challenges to come.

"What we're seeing is a historically significant scale up of a chronic disease treatment program," says **Jim Yong Kim**, MD, PhD, director of the HIV/AIDS Department at the World Health Organization (WHO) in Geneva. Kim and other world health officials spoke about the progress in providing HIV treatment worldwide at a teleconference held in June.

"The HIV treatment scale up is surely the most ambitious project in the history of global public health," he says. "However, we don't believe that progress has been fast enough."

There are an estimated 6.5 million people in developing nations who need antiretroviral treatment, says **Ties Boerma**, PhD, director of WHO's department of measurement and health information systems. Boerma also spoke at the teleconference.

The 6.5 million figure includes all people who are in the last two years of their infection, he says.

"So we've also estimated that 660,000 children are in need of treatment," Boerma adds.

WHO and UNAIDS set a goal called the "3 by 5" initiative two years ago, in hopes of bringing 3 million people in developing nations into antiretroviral treatment by 2005. With 2 million remaining on the goal at the midyear point, it does not appear the goal will be met, Kim says.

"While we don't think we're going to make the target, there are tremendously exciting things happening in many, many countries," he says.

A June report by WHO and UNAIDS, called Progress on Global Access to HIV Antiretroviral Therapy — An Update on "3 by 5," describes these hallmarks of the program's success:

- Zambia, which has an epidemic that has resulted in HIV infection among 16% of the population, with women constituting 54% of the people living with HIV/AIDs, now has 600,000 orphans as a result of AIDS deaths. In October 2004, the president of Zambia announced a plan to provide antiretroviral drugs for free at public institutions; and as of March 2005, the government reported distributing antiretroviral therapy to 22,000 people, adding about 1,000 people a month to the treatment list. WHO now estimates that between 26,000 and 30,000 people in Zambia are receiving HIV antiretroviral therapy.
- Mozambique has more than 1.1 million people living with HIV/AIDS, about 12% of the adult population, and there are estimates the country's HIV/AIDS toll will grow to 1.8 million by 2007. Despite years of civil conflict and a weak health infrastructure, the nation is scaling up its antiretroviral treatment program.

"The Minister of Health of Mozambique when he visited us during the World Health Assembly told us that they've now been convinced that treatment programs based on clinical officers and nurses who are supervised by physicians are very effective," Kim says. "So they have begun training their high school graduates, among whom

they have a terrible unemployment problem."

• The HIV epidemic in Indonesia, with about 110,000 people infected, has grown rapidly among injecting drug users, reaching a prevalence rate of 53% among IDUs in Bali and 48% among IDUs in Jakarta. The Indonesian government has committed to bringing 10,000 people into treatment by the end of 2005. The government also issued in October 2004 a compulsory license for the production of two antiretroviral drugs, and 25 antiretroviral referral sites were initiated in 13 provinces of Indonesia. The country also has established pilot methadone programs in Jakarata and Bali, including prison methadone programs.

The world health community's focus on expanding antiretroviral treatment has led to some important changes in prevention and testing.

"There's an incredible upsurge in the demand for testing, and what's happened because of these expanded treatment programs is that we're doing testing in a different way," says **Paul De Lay**, MD, director of evaluation at UNAIDS.

"We are offering tests to those who are most likely to need them — TB patients, patients with sexually transmitted diseases, people with illnesses that are within the range of an AIDS diagnosis in an outpatient clinic, sick people in an inpatient hospital ward situation," he explains.

UNAIDS estimates the cost of scaling up antiretroviral treatment in developing countries will reach $22 billion by 2008, a number that includes the cost of refurbishment of health centers and recruiting new health providers , De Lay says.

WHO and UNAIDS officials acknowledge that part of the reason the 3 by 5 goal has not been reached is because of unanticipated challenges, including problems with the drug delivery system.

"What we call procurement and supply chain management is a major issue," Kim says. "I don't think any of us really thought that it would be as big an issue as it's become."

These problems often are as simple as a country lacking a warehouse with a lock where the drugs could be safely stored.

Also, many countries are faced with the reality of dealing with a volume of need for antiretrovirals that surpasses any other medical need they've handled, Kim notes. "So it's things like this, the small details that we just got a late start on that didn't get here."

The majority of developing countries have had difficulty getting their systems up and running, says **Bernard Schwartlander**, MD, director of strategic information and evaluation for the Global Fund to Fight AIDS, Tuberculosis, and Malaria. However, improvements are being made, he says.

For example, in India there have been major resources from the Global Fund, and there has been a major initiative launched with the Clinton Foundation, Schwartlander reports.

"I think for India, we're going to have to look at creative and innovative solutions," Kim says. "What we hope to see is vastly improved numbers in terms of physicians and nurses who understand antiretroviral treatment, and that's through the Clinton Program."

Plans are to train 100,000 people in the next couple of years, he adds.

Another challenge of providing antiretroviral treatment to developing nations is that whether it's one in six or one in three people in need of drugs who receive the help, there has to be some ethical system for deciding who will receive the treatment, Kim notes.

"We thought very hard about this, and we convened meetings of the top medical ethicists in the world and really asked them this question," he says. "What they said was what we can do as ethicists is offer to countries and even communities a set of three or four different scenarios of how they might go about selecting who gets treatment first."

There are many ways to make this decision, Kim says, including these:

• "You can look at the severity of the symptomology, how sick people are," he says.

• "You can look at health workers, for example, is a case that's been made in some countries, that in order to care for the rest, we need to get the health workers on treatment," Kim says.

Most of the countries have responded to these suggestions by asking for general boundaries, including what the world health community feels is absolutely unethical, and then they'll think about it and come up with their own approach, he explains.

The result has been that many nations are making decisions based on local criteria, Kim says.

So far it appears that at least with regard to gender issues, the distribution of drugs is encouraging, as early data show that about half of the people on treatment are women, he reports.

"So that should not let us drop our guard because what we've also seen is that the enrollment of women is much higher in places where access to care is free at the point of delivery," Kim says. "So we've got to keep counting, and we've got to give general guidelines, but then it's really countries, communities, and organizations that will make the final decision." ■