

# SPECIAL COVERAGE AIDS ALERT

XIII International AIDS Conference - Durban, South Africa

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### Special Issue: XIII International AIDS Conference

## Perfect vaccine for HIV not likely, researcher warns

*Advances in science have helped effort*

*(Editor's note: This special issue of AIDS Alert contains exclusive coverage of the XIII International AIDS Conference, held July 9-13 in Durban, South Africa. More than 15,000 physicians, scientists, clinicians, and other health care providers from around the world attended the biennial conference that is intended to provide a forum for education and sharing knowledge regarding the AIDS crisis.)*

Unlike traditional vaccines that prevent infection, in the case of HIV, a vaccine that would prevent AIDS or even delay the progression of the disease would be a tremendous achievement, said **Margaret Liu, MD**, vice president for Vaccines Research and Gene Therapy at Chiron Corp. in Emeryville, CA.

Liu said the clinical goal for an HIV vaccine differs from other vaccine projects because of the urgent need to make an impact on the global pandemic, but she cautioned scientists against setting their sights on the perfect vaccine.

"For a pathogen such as HIV that is capable of entering the genome of cells, the challenge to make a vaccine that would prevent any infection at all is indeed great and may be too big a first step," she said during her address at the XIII International AIDS Conference, held in Durban, South Africa.

The search for a suitable HIV vaccine faces enormous challenges. "At the start of this epidemic, no

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The long wait for a rapid HIV test may be over early next year, as one of the more promising tests begins studies at 20 U.S. sites. The OraQuick HIV-1/2 rapid HIV test was introduced at the XIII International AIDS Conference. It collects oral fluid in 15 seconds, presents test results in 20 minutes or less, requires no needles, is simple to use, and has demonstrated an accuracy of more than 99% . . . . . 115

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■ **More bad news about PIs:** A San Francisco hospital has discovered that HIV patients taking protease inhibitors have a higher incidence of a certain type of bone disease

■ **New research overseas on connection between TB, AIDS:** There's a definite link between HIV and tuberculosis pandemics, according to the latest research

**Special Issue:  
XIII International AIDS Conference**

one even knew enough about the virus or immunology to know what questions to ask," Liu said.

Advances in the fields of virology, immunology, and cell biology during the past two decades have added impetus and knowledge to the vaccine effort, Liu said.

"Although we don't fully understand correlates of immunity or how and where to generate immune responses, we have gained many insights from animal studies and human populations. These inform and guide our vaccine development efforts," she said. "Secondly, while we have accumulated a great deal more knowledge, for example, regarding the genotype of different strains, we still have much to learn."

Liu cautioned that researchers should not be dogmatic and always should be guided by the proof provided by scientific data. "We must be careful to not make any assumptions, for example, about which strains to use for vaccines that would hinder the development of an effective candidate."

***Progress looks promising for vaccines***

Advances made so far are encouraging, Liu said. They include the elucidation of immune responses in highly exposed uninfected individuals, such as commercial sex workers, and in patients whose disease did not progress as rapidly as expected, the so-called "long-term nonprogressors."

"These individuals provide evidence for the power of the immune response to contain and restrain the viral infection. Likewise, their immune responses provide clues as to what a vaccine should elicit," she said.

Great progress also has been made illuminating the structure of HIV and in understanding what processes and structures need to be interfered with in order to prevent infection or its spread, Liu said. "And of course, given the types of immune responses that are thought necessary for an HIV vaccine, the novel and dramatic advances in vaccine technologies promise to provide the means for making an HIV vaccine."

A range of vaccine candidates are in the early stages of development. Some of those are live virus vaccines, viral vectors, and gene-based

vaccines such as plasmid DNA vaccines. Still others being evaluated are vaccines combining more than one type of entity (the mixed-modality vaccines) and protein-based vaccines using other forms of envelope or other viral proteins, along with more advanced candidates such as the recombinant envelope glycoproteins, which are currently in phase III efficacy trials.

### ***Renewed efforts to induce cellular responses***

Turning to the issue of the progress made by studying humans who had generated effective human responses against HIV, Liu said that those individuals had provided evidence of “natural immunity” that could have considerable efficacy and appeared to have been generated by exposure to and/or infection by either HIV-1 or HIV-2.

Recently, there have been increased efforts in vaccine research to induce cellular responses instead of or in addition to antibody response, Liu said. Those approaches were based on the rationale that because T lymphocytes recognize pieces of the virus displayed on the surface of infected cells, the T-cell responses could be directed against conserved regions of the virus. In addition, cellular responses appeared to play a role in controlling HIV.

One way to make a vaccine that has broad efficacy against different strains of the virus might be to take advantage of the conservation of certain proteins or regions of proteins among different strains, she noted, even if the protein is on the viral surface where it might be susceptible to antibody targeting.

### ***Scientists have a better understanding***

The ability of cytolytic T lymphocytes (CTL) to kill HIV-infected cells is not the only mechanism for cellular immunity. “The multiple mechanisms of cellular immunity provide another reason for efforts to induce cellular responses,” Liu said. “In addition to killing virus-infected cells, CTL releases molecules that may play a crucial role for a preventive or therapeutic AIDS vaccine. And, of course, cellular responses include helper as well as cytolytic T-cells.”

Important advances have been made in understanding the virus, she said. “Our global battle

against HIV is nothing less than a war, and just as in war, where it is important to understand the enemy in order to outsmart it, we must understand HIV, what its structure is like, and how it infects and causes diseases in order to be able to defeat it.”

A lot has been learned about HIV and how it causes disease, said Liu, but researchers need insights into how to induce antibodies that will broadly neutralize viruses both within a clade and between clades. They should not assume that making a vaccine from one clade would be the solution for all the strains within that clade.

Likewise, researchers should not assume that novel immunogens made starting from one clade would not induce antibodies, which can neutralize virus from another clade. Those decisions must be based on scientific data, said Liu, and not on assumptions. ■

## **Microbicides may increase risk of contracting HIV**

### ***Unfavorable results of trial considered setback***

**T**he spermicide nonoxynol-9 is ineffective against HIV and may even increase the risk of transmission, according to results of a UNAIDS-sponsored study released at the XIII International AIDS Conference in Durban, South Africa.

The findings of the triple-blind multicenter trial are considered a setback in microbicide research, which until now has received scant support from the private sector and is largely funded by development agencies and nongovernmental organizations.

Microbicides are chemical substances — in the form of gels, creams, suppositories, or films — that kill viruses and bacteria when applied vaginally or rectally before sexual intercourse.

Trial co-coordinator **Lut van Damme**, MD, MSc, of the Institute of Tropical Medicine in Antwerp, Belgium, said all of the women enrolled in the trial had received intensive condom counseling, free treatment for all sexually transmitted diseases, and regular checkups. Commercial sex workers in Benin, Cote de Ivoire, South Africa, and Thailand

were chosen at random from a pool of volunteers who were informed of the risks and who agreed in writing to take part in the tests.

Van Damme said the main objective of the study was to ascertain whether there was a statistically significant difference in the incidence of HIV infection between the two groups of women.

Nonoxynol-9, which is marketed in the United States and China under the trade name Advantage S, is a spermicidal agent used in contraceptive spermicide products and as a complementary component in the lubricant of barrier methods of contraception, such as the male condom.

“We wanted to assess the efficacy of the gel, the long-term safety of its use, and its impact on transmission of HIV to women during sexual intercourse,” said Van Damme.

### ***Scientists issue warning to users of product***

In the first analysis of the results of seroconversion and HIV incidence among the 990 women who took part in the trials, the researchers found that there was a 15% incidence in the nonoxynol-9 group, compared with 10% in the placebo group, said Van Damme. Women using nonoxynol-9 also exhibited more lesions than those in the placebo group.

“We were dismayed to find out that the group of women using nonoxynol-9 had a higher rate of HIV infection than the group using a placebo,” said **Joseph Perriens**, MD, PhD, who heads the UNAIDS microbicide effort.

The active group had 59 infections, while the placebo group had 41. “This is a significant difference,” he explained. “With the incidence of HIV infection in both groups in this study lower than that seen in the untreated population from which volunteers were recruited, it is clear that the rate of infection was greater with the nonoxynol-9 gel compared to its placebo control preparation.”

He issued a warning to women at high risk of HIV infection to not use the product because the bulk of evidence suggested that it was either ineffective or harmful as an anti-HIV agent.

Despite the setback, Perriens called for renewed effort and continued commitment to microbicide research. “We have lost one battle, but we have a

war ahead of us,” he said. “And we think it can be won.”

Perriens announced that UNAIDS would call for an acceleration of the introduction of new and more promising microbicide candidates in large-scale phase III trials. Three more products are currently in advanced safety testing and could be available for inclusion in combined safety/efficacy evaluation within months. The safety testing of 10 additional products, including two antiretrovirals, also should be accelerated, he recommended.

Some of those products work by irreversibly inactivating HIV by perforating or disintegrating the virus’s outer membrane. Others block the virus’s attachment to receptors on the cell surface or prevent its replication within the cell by inhibiting the action of reverse transcriptase, an enzyme needed by the virus to establish itself within the cells it infects. Laboratory studies have shown all of those approaches to be highly effective against HIV. Many also are active against sexually transmitted disease pathogens such as *Neisseria gonorrhoea*, *Chlamydia trachomatis*, and the virus responsible for genital herpes.

**Alan Stone**, MD, chairman of the International Working Group on Microbicides in London, said

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“We were dismayed to find out that the group of women using nonoxynol-9 had a higher rate of HIV infection than the group using a placebo.”

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considerable resources need to be mobilized to develop microbicides. While 10 public agencies currently are members of the International Working Group, research efforts have been hampered by a lack of funding, leaving many promising leads stuck in the pipeline.

The role of the International Working Group is to facilitate the development and approval of microbicides, which need to be safe as well as effective, affordable, and acceptable to the user.

Adding weight to Perriens’ claim that this type of research is largely underfunded, Perriens said the U.S. government has invested \$25 million in microbicide research, which accounts for only 1% of its total investment in HIV/AIDS research.

**Awa Coll-Seck**, the director of policy, strategy, and research at UNAIDS, emphasized the importance of microbicide research, saying it is a method that “can allow women to protect themselves and their partners from infection without necessarily having to secure male cooperation.”

A report by the International Working Group says that while condoms can provide an excellent level of protection if correctly and consistently used, many people — particularly women in socially vulnerable positions — find it difficult or impossible to persuade their partners to use them. ■

## Present drugs not expected to kill virus

*Scientist envisions future of simpler regimens*

The pendulum will swing back toward later treatment of HIV-infected patients, and the definition of failure of clinical trials will be revisited, predicted **Mauro Schechter**, MD, PhD, professor of infectious diseases at the Hospital Universitario Clementino Fraga Filho at Federal University of Rio de Janeiro in Rio de Janeiro, Brazil.

Schechter, who addressed the XIII International AIDS Conference in Durban, South Africa, and made predictions about what would happen by the time the international conference reconvenes in 2002 in Barcelona, foresees a greater emphasis on “delta viral load,” the renaissance of CD4 count as a guide to therapy, and the availability of simpler drug regimens.

He also spoke about a renewal of interest in the prevention of opportunistic infections, which in turn will take into consideration local epidemiological conditions.

Schechter’s address re-emphasizes the point made by Anthony S. Fauci, MD, director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health in Bethesda, MD, that the eradication of the virus with currently available drugs is unlikely.

Since the Geneva conference two years ago,

data have accumulated showing that virologic failures are more common in practice than in trials and that opportunistic infections occur at

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The conference address by Mauro Schechter, MD, PhD, stresses the point made by Anthony S. Fauci, MD, that the eradication of the virus with currently available drugs is unlikely.

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similar CD4 cell counts in patients who are on therapy and those who are not, Schechter said. Although many patients did not achieve full immune recovery, a large proportion did achieve a “safe” level of immune competence, he added.

On a more cautionary note, he said antiretroviral therapy was associated with potentially serious side effects, some of which might be time-dependent.

Those newly acquired data have led to renewed debate on the optimum time to treat, the choice of initial drug regimens, when to change and how to sequence them, and how to simplify existing regimens, Schechter said. Emphasis has shifted to the role of new drugs, pharmacological enhancement in extending treatment benefits, and management and prevention of opportunistic infections.

### *Slope of viral load similar in some patients*

In the course of his presentation, Schechter reviewed recent data on a wide range of issues related to HIV/AIDS treatment, making reference to the contested debate about the optimal time to initiate therapy, particularly in connection with threshold values of viral load and CD4 cells.

With regard to viral load, two recently published reports demonstrated a direct association between the slope of the increase of plasma viral load in the first few years after seroconversion and the probability of progressing to AIDS. “It was also shown that for those who progressed to AIDS, the slope of viral load increase in the three years preceding progression to AIDS was similar, regardless of prior AIDS-free time,” Schechter said.

These observations argue against a blanket concept of a fixed set point, said Schechter. They also suggest that it may be more appropriate to measure viral load in a serial fashion, rather than relying on one or two measurements to make therapeutic decisions.

Schechter referred to a report to be presented at the conference by Julio Montaner, MD, national co-director of the Canadian HIV Trials Network, Ottawa, Ontario, on a population-based cohort analysis of antiretroviral naive patients in British Columbia who started HAART between August 1996 and September 1999.

### ***Postponing therapy OK if immune levels safe***

Results from the study, which involved 1,200 eligible participants, showed that effectiveness of therapy is dependent on baseline CD4 count, not on age, gender, viral load, prior AIDS diagnosis, or protease inhibitor (PI) use. "Furthermore, few patients with baseline CD4 > 200 cells/mm<sup>3</sup> experienced clinical progression, and progression rates were similar for patients with CD4 counts of 200-350 or 350-500 cells/mm<sup>3</sup>.

The study also showed that it is probably correct to postpone treatment initiation as long as therapy is started while immune recovery to "safe" levels is still possible. However, the question of how to define this moment precisely remains unanswered.

### ***Less-potent regimens likely in future***

Schechter's address tracked the progress made in the past two years but emphasized that many earlier conclusions had yet to be revisited. In summing up, he predicted that the future would see a re-evaluation of "less potent" regimens, particularly of their cost-effectiveness in resource-limited settings, which was a major focus of the conference.

Structured treatment interruptions would be discussed as a means of making treatment less toxic and more affordable, and pressure on industry and governments would increase to ensure equal and universal access to antiretroviral therapy, which is still unavailable to the majority of those infected with HIV in the developing world, Schechter said. ■

## **HAART interruption may control HIV long-term**

### ***Large amount of HIV produced after infection***

**T**he interruption of highly active antiretroviral therapy (HAART) may be a means of long-term control of HIV in AIDS patients, said **Anthony S. Fauci**, MD, at the XIII International AIDS Conference in Durban, South Africa.

"Unfortunately, prolonged courses of continuous HAART are not an option for most HIV-infected individuals because of the short- and long-term problems associated with a variety of regimens," said Fauci, director of the National Institute of Allergy and Infectious Diseases at the National Institutes of Health in Bethesda, MD. "With current drugs, it is almost certainly not feasible to have people on therapy for an indefinite period of time. Therefore, new approaches have to be undertaken."

### ***Studies prompt review of long-term therapy***

The re-thinking of the philosophy of therapeutic approaches to long-term treatment of HIV is based on a number of studies, including one by the National Institute of Allergy and Infectious Diseases, that have found that a reservoir of HIV is established soon after primary infection.

"The reservoir consists at least in part of resting, latently infected CD4+ T-cells distributed in various lymphoid organs throughout the body. The presence of latently infected CD4+ T-cells is relevant to previous projections regarding the possibility of eradicating HIV infection," Fauci said.

He referred to an earlier model of viral dynamics demonstrating that a considerable proportion — 93% to 99% — of plasma virus emanated from recently infected, rapidly turning over, productively infected CD4+ T-cells. The model, developed in part by David Ho, MD, head of Aaron Diamond AIDS Research Center in New York City, had a lesser amount — 1% to 7% — of plasma virus that came from long-lived cell populations.

"An immeasurably small proportion of the plasma virus comes from latently infected CD4+ T-cells," Fauci said.

While the presence of those cells was not particularly relevant during the period of uncontrolled bursts of viremia, he said, it was relevant during the aviremic state induced by HAART in many individuals.

Studies have shown that despite what had seemed to be the adequate control of the virus by HAART, virus replication was likely ongoing and possibly contributed to the maintenance or reconstitution of the latently infected pool of resting CD4+ T-cells.

“When individuals are receiving HAART, viral spread is contained, and hence an aviremic state persists,” he said. “However, when individuals are taken off HAART, within a couple of weeks, high levels of virus expression are seen in the lymphoid tissue.”

### *Jury out on impact of repeated interruptions*

Fauci said interrupting therapy had been used to determine whether HIV had been eliminated. “It was clear we had to deal seriously with the existence of a persistent pool of latently infected, resting CD4+ T-cells in HIV-infected individuals, even those who had been effectively treated with HAART.”

The approach of interrupting therapy for variable periods of time is a subject of intense investigation worldwide, Fauci said. “There are several approaches to this. One is the single interruption of therapy without cycling. Another falls under the rubric of strategic or structured therapy interruptions [STIs]; one such approach resumes therapy after interruption only when plasma viremia reaches a predetermined level, while another is to discontinue and resume therapy at predetermined times to do cyclic interruptions.”

Initial studies had shown that with a single discontinuation of therapy, the virus came back with a vengeance within four weeks in most patients, but only rarely within the first seven days off therapy, Fauci said. Based on that, he looked at what happened if therapy was interrupted every other week. He found that the virus did, in fact, come back after discontinuation of therapy, but in no individual did it go above several hundred copies per mm<sup>3</sup>.

“Over a seven-cycle or eight-cycle regimen, we found striking differences between individuals

who had HAART interrupted every other week, compared to those who had therapy interrupted every two months,” he said.

Plasma viremia rebounded in virtually all HAART-treated patients in whom therapy was interrupted, and levels of HIV-specific CD8+ T-cells also rebounded in parallel with the return of plasma viremia.

Repeated interruptions of HAART could lead to prolonged intervals before viral rebound and or lower peaks of rebound due to residual HIV specific CD8+ T-cells or other immune responses left over from previous viral-induced stimulations, he said. “This delay in rebound of plasma viremia may allow for significant periods of time off therapy.”

However, he said it was doubtful whether a specific percentage of patients who originally had progressed prior to therapy would be able to have HAART discontinued for prolonged periods of time following repeated interruptions.

Fauci concluded by saying that the precise role and mechanisms of the HIV-specific immune control of HIV during repeated interruptions of therapy had not yet been delineated. He also said the long-term effect of interruptions of HAART on the emergence of resistance mutations and the ultimate clinical course of patients remained to be determined. ■

## Complacency reversing gains in war against AIDS

### *Drug advances are culprits in ongoing battle*

**A**ntiretroviral drugs are creating complacency in some developed countries, reversing gains in the AIDS epidemic, said **Roy M. Anderson**, FRS, of Wellcome Trust Centre for the Epidemiology of Infectious Disease at the University of Oxford in Oxford, England.

“Complacency is the main worry in many Western countries for the coming decade, with increases in risk behavior already apparent in young gay men as reflected, for example, in the rise in the incidences of various sexually transmitted diseases such as rectal gonorrhoea in San

Francisco and a concomitant recent rise in the incidence of HIV,” Anderson said in his address at the XIII International AIDS Conference in Durban, South Africa.

Anderson attributes the problem partly to the perception that AIDS is a treatable condition with the advent and success of combination drug therapies. He said the slow and steady increase in the incidence of HIV in heterosexuals and the explosive epidemic of AIDS in many Eastern European countries also are of major concern.

### ***Success of public health campaigns varies***

Public health authorities, therefore, face many challenges in the coming decade, said Anderson. Those include:

- the intensification of AIDS educational campaigns for the young;
- combating the spread of drug-resistant strains of the virus;
- promoting good adherence to recommended drug regimens for those infected and on combination drug therapy;
- finding the necessary resources for enhanced surveillance to detect a higher percentage of infections early on;
- stimulating more research in the development of vaccines.

Anderson said successful public health campaigns have reduced the impact and spread of HIV, but progress varies in different countries. While Sweden has made remarkable progress in limiting the spread, Spain and certain areas of the United States have achieved much less success, he said.

“Each country has a unique epidemic formed from varying contributions by infections in gay men, IV drug users, and heterosexuals,” he said.

While little variability occurred in general patterns of the distribution of age-related sexual partner acquisition, much heterogeneity exists in patterns of mixing within and between major risk groups and the degree to which educational messages have penetrated certain sectors of society in different industrialized countries, said Anderson.

Many success stories — ranging from effective needle-exchange programs to frequent use of condoms to the reduction in the number of new

sexual partners — have been recorded. Drug therapy also has significantly reduced the likelihood of vertical transmission of the virus.

“What typifies the most convincing cases is the quantitative study of behavior change, concomitant with the monitoring of HIV incidence and seroprevalence,” Anderson said.

He said the widespread use of highly active antiretroviral therapy (HAART) during the past five years in developed countries has had a significant impact on the incidence of AIDS, a change concomitant with an increase in the pool of HIV-infected persons as combination therapy prolonged the lives of those infected. However, it also brings the associated risks of an enhanced net rate of transmission.

And while aggressive drug therapy could lower viremia to undetectable levels and bring improvements in immune status, even the combination of five drugs does not seem to eliminate the virus from the host, he said.

Cessation of therapy, therefore, typically results in rapid growth of the virus and associated diseases, Anderson said, while poor adherence to treatment has created multidrug-resistant strains that are difficult to treat.

“Tight adherence to prescribed drug regimens is key to long-term suppression of viral load. Since the net rate of viral evolution is proportional to total viral load, poor adherence early on post the initiation of combination therapy, when viral load is declining from high levels, carries the greatest risk of the evolution of resistance. Once viral load is very low, a short period of poor adherence is less serious,” he explained.

“However, the general messages for those on treatment are that good adherence is vital, as is the adoption of safe sex practices at all times,” he added.

The development of vaccines is seen as a long-term solution to the epidemic, but Anderson cautioned that the path to that goal will be difficult, largely due to the great genetic diversity of the virus and its propensity for rapid evolution.

“The clear need is for action now, at a scale and degree of international collaboration not seen before in the history of the fight against infectious disease,” he said. “International collaboration and political leadership are key ingredients for promoting this goal.” ■

## Genetic diversity needs further examination

*More research required before developing vaccine*

While continued research into the genetic diversity of HIV-1 in West and West Central Africa is necessary, the implications for a vaccine are clear in a preliminary study, researchers said at the XIII International AIDS Conference in Durban, South Africa.

**Martine Peeters**, PhD, of the Institute for Research and Development in Montpellier, France, says that research conducted in eight countries identified and characterized more than 1,500 HIV-1 viruses in West and West Central Africa and found that the predominant subtype is A.

Peeters presented a paper on behalf of five other members of the research team during the conference. For the purposes of the research, data were collected between 1997 and 1999 in Senegal, Mali, Niger, Nigeria, Chad, Cameroon, Gabon, and the Democratic Republic of the Congo.

### *Different subtypes occurring across Africa*

Peeters said that the A subtype decreased in prevalence from the West, where it was found in about 85% of the cases studied, to less than 50% in West Central Africa. Subtype G was recorded in all the countries and represented more than 25% of the viruses in Nigeria. A higher diversity was found in countries situated in West Central Africa, such as the Democratic Republic of the Congo. In those countries, there were more subtypes, more recombinants, and a higher diversity within subtype A.

The majority of known HIV-1 subtypes and circulating recombinant forms were present in all the countries studied, but their prevalence varied, Peeters said. In addition, there were differences in the subtype of HIV-1 prevalent within the countries studied. For example, in Zaire, he said, one subtype was most prevalent in the North, while another was more prominent in the South.

Genetic subtype distribution is a dynamic process, a factor that is important for vaccine strategies, he emphasized. However, further analysis of

the results is needed and other recent information must be analyzed when considering a vaccine.

In other research, a study of HIV-1 subtype C viruses has culminated in the selection, based on genotypic and phenotypic properties, for inclusion into HIV-1 candidate vaccine.

It is anticipated that the first phase of trials will start next year, said **Carolyn Williamson**, MD, of the department of medical microbiology at the University of Cape Town in South Africa.

Samples of HIV-1 subtype C, which is prevalent in about 90% of the HIV infections in Southern Africa, were collected from commercial sex workers in the KwaZulu-Natal province. The sex workers saw an average of about four clients a day, and most did not use condoms. They had seroconverted at least one year before the samples were collected.

Williamson said the phylogenetic analysis classified all 31 isolates as subtype C based on gag, pol, and env genes.

“Two isolates were selected for inclusion into vaccines based on phylogenetic analysis, amino acid similarity to the consensus sequence, R5 phenotype, and adequate replication capacity in tissue culture,” she explained.

Research into HIV-1 diversity in South America has found that subtype B continues to be the most prevalent genotype of HIV-1 in most of the eight countries surveyed. However, a surprisingly high prevalence of subtype F was detected, said **Kevin Russell**, MD, head of the department of virology of the United States Navy Medical Research Center Detachment in Lima, Peru.

### *Virus starting to take hold of South America*

Russell was the presenting author of a paper on research conducted by 12 individuals from Peru, Uruguay, Paraguay, Argentina, Ecuador, Bolivia, and the United States. The study was conducted in collaboration with the Pan American Health Organization, respective health departments in the various countries participating in the research, and nongovernmental organizations that could play a role.

Russell said the Navy Medical Research Center Detachment has been involved in HIV surveillance in South American countries since the early 1990s, but it dramatically increased its scope in

1998, when new aspects and attitudes relating to AIDS were detected.

Poverty and the lack of empowerment of women were important factors in this area, Russell noted, where an estimated 150,000 new infections occurred last year. "Now is the time for intervention and education to have an impact," he says.

Russell added that knowledge of circulating genotypes of HIV-1 is becoming increasingly important as vaccine trials become a reality.

From eight at-risk populations in five countries, the prevalence of HIV ranged from 0.3% to 21%. Genotype B was found to be predominant in five of the six countries from which 825 samples were collected for genotyping. Of the total samples processed, 77% were genotype B, 23% genotype F, and there was only one instance each of genotypes C and A.

One exception to the prevalence of subtype B, Russell says, was in Argentina. In that country, researchers found that the majority of maternity patients who were HIV positive were genotype F. A similar discrepancy was obtained in the data from Uruguay, where nearly half of the infections identified were genotype F.

### ***Subtypes rapidly expanding in France***

Russell said continued surveillance of HIV in South America is clearly warranted. "The epidemic in South America is in its early stages. Now is the time to target groups to ensure early intervention."

In France, the population infected by the subtype B has remained phylogenetically stable, but a fast introduction of new subtypes has been experienced. A 16% prevalence of non-B subtypes was recorded in 295 patients, but those were mainly from Africa or were people who had African partners.

Those were the findings of a study presented by Pierre Roques of the Centre for Experimental Atomique in France. The research was conducted by a team of eight and involved the testing of 2,168 HIV-1 positive patients.

In a subgroup, the year when HIV infection occurred was estimated. From that group of 552 HIV-1 positive patients, 483 were infected with subtype B, and 69 with a non-B subtype. ■

## **CDC: HIV risk behaviors on rise while therapies show chink in armor**

*Experts say it's time to regain control of epidemic*

The HIV epidemic in the United States clearly has been overshadowed in recent months by the frightening statistics and predictions about the African continent's AIDS war. But before Americans become too complacent with success stories about HIV and the protease inhibitors and other antiretrovirals, they should heed the warning signs apparent in the latest government HIV research.

Studies sponsored by the Centers for Disease Control and Prevention (CDC) in Atlanta raise some alarming questions. Research indicates that antiretroviral therapy does not succeed in all patients, and it must be improved continuously to maintain long-term suppression. CDC investigators also have found much evidence that Americans are not taking the AIDS threat as seriously as they have in the past, which means prevention efforts need renewed and stronger impact on at-risk populations.

"We've said all along that these drugs are a cure for no one, and they don't work for everyone," said **Julio Abreu**, deputy director of government affairs at AIDS Action in Washington, DC.

While antiretrovirals certainly have brought down the rate of AIDS deaths nationwide, the protease inhibitors and combination therapies haven't been around long enough for researchers to study the long-term efficacy. Also, no one knows the health effects that the drugs have on people who have been taking them for many years, Abreu added.

"We still believe prevention is the best way to deal with this epidemic," he said. "Prevention costs less, and it's more humane for folks not to get this deadly disease in the first place."

Together, each of the CDC's new studies becomes one part of a bigger puzzle that shows

*(Continued on page 109)*

## Estimates of the number of people living with AIDS as of June 1999, by state of residence: Comparison of three methods

State of residence	Ryan White CARE Act		Number reported to be living		Adjusted for reporting delays	
	Number*	Percent	Number*	Percent	Number*	Percent
Alabama	2,459	0.9	2,669	0.9	2,792	0.9
Alaska	194	0.1	234	0.1	234	0.1
Arizona	2,787	1.0	2,584	0.9	3,211	1.0
Arkansas	1,119	0.4	1,369	0.5	1,443	0.5
California	39,408	14.0	41,649	14.5	44,677	14.5
Colorado	2,328	0.8	2,633	0.9	2,715	0.9
Connecticut	4,627	1.6	5,293	1.8	5,653	1.8
Delaware	1,034	0.4	1,022	0.4	1,079	0.3
District of Columbia	4,630	1.6	5,360	1.9	5,788	1.9
Florida	30,237	10.8	32,699	11.4	32,945	10.7
Georgia	8,627	3.1	9,376	3.3	10,103	3.3
Hawaii	815	0.3	882	0.3	915	0.3
Idaho	191	0.1	199	0.1	205	0.1
Illinois	8,723	3.1	8,137	2.8	8,926	2.9
Indiana	2,345	0.8	2,363	0.8	2,448	0.8
Iowa	479	0.2	545	0.2	574	0.2
Kansas	868	0.3	850	0.3	895	0.3
Kentucky	1,405	0.5	1,390	0.5	1,526	0.5
Louisiana	4,936	1.8	4,937	1.7	5,170	1.7
Maine	316	0.1	386	0.1	428	0.1
Maryland	8,804	3.1	8,650	3.0	9,520	3.1
Massachusetts	5,502	2.0	5,398	1.9	6,672	2.2
Michigan	4,136	1.5	4,014	1.4	4,471	1.4
Minnesota	1,262	0.4	1,458	0.5	1,507	0.5
Mississippi	1,783	0.6	1,733	0.6	1,815	0.6
Missouri	3,163	1.1	3,853	1.3	4,030	1.3
Montana	130	0.0	150	0.1	167	0.1
Nebraska	409	0.1	425	0.1	438	0.1
Nevada	1,791	0.6	1,972	0.7	2,024	0.7
New Hampshire	325	0.1	454	0.2	466	0.2
New Jersey	14,872	5.3	13,703	4.8	14,206	4.6
New Mexico	806	0.3	844	0.3	912	0.3
New York	50,993	18.1	49,036	17.0	54,664	17.7
North Carolina	4,005	1.4	3,900	1.4	4,249	1.4
North Dakota	44	0.0	42	0.0	43	0.0
Ohio	4,120	1.5	3,881	1.3	4,160	1.3
Oklahoma	1,286	0.5	1,470	0.5	1,526	0.5
Oregon	1,660	0.6	1,843	0.6	1,948	0.6
Pennsylvania	9,359	3.3	9,611	3.3	10,741	3.5
Puerto Rico	9,259	3.3	8,597	3.0	9,008	2.9
Rhode Island	773	0.3	835	0.3	877	0.3
South Carolina	3,978	1.4	3,918	1.4	4,121	1.3
South Dakota	70	0.0	63	0.0	62	0.0
Tennessee	3,443	1.2	3,808	1.3	4,058	1.3
Texas	20,326	7.2	21,869	7.6	22,676	7.4
Utah	728	0.3	847	0.3	870	0.3
Vermont	138	0.0	161	0.1	172	0.1
Virgin Islands	200	0.1	207	0.1	222	0.1
Virginia	5,091	1.8	5,001	1.7	5,569	1.8
Washington	3,184	1.1	3,659	1.3	3,803	1.2
West Virginia	450	0.2	431	0.1	459	0.1
Wisconsin	1,274	0.5	1,454	0.5	1,485	0.5
Wyoming	56	0.0	62	0.0	65	0.0
<b>Total</b>	<b>280,958</b>		<b>287,946</b>		<b>308,933</b>	

\* Cumulative from July 1989 through June 1999.

+ Cumulative from 1981 through 1999.

## AIDS cases reported July 1989 through June 1999, by state of residence

State of residence	7/89-6/90	7/90-6/91	7/91-6/92	7/92-6/93	7/93-6/94	7/94-6/95	7/95-6/96	7/96-6/97	7/97-6/98	7/98-6/99
Alabama	204	318	425	702	557	564	663	523	604	467
Alaska	29	16	14	29	73	79	37	44	41	30
Arizona	370	237	368	1099	644	556	655	531	546	738
Arkansas	116	220	197	423	289	286	283	242	227	189
California	6781	7343	8386	15059	14155	10813	10440	8079	6283	5737
Colorado	378	442	423	1080	882	715	597	431	316	339
Connecticut	435	480	480	1462	1306	1057	1513	1201	892	622
Delaware	83	90	106	307	258	309	318	264	161	177
District of Columbia	535	712	813	1077	1575	1216	1050	1191	941	750
Florida	3969	4862	5193	8999	7651	9225	7664	6674	5410	5683
Georgia	1219	1197	1735	2246	2242	2294	2489	2102	1368	1635
Hawaii	190	185	165	201	316	263	207	144	128	140
Idaho	23	23	39	66	55	57	44	44	39	29
Illinois	1228	1216	1837	2810	2725	2752	2140	1749	1765	1285
Indiana	329	283	378	757	724	520	651	560	484	353
Iowa	48	89	86	189	98	144	128	104	97	73
Kansas	133	113	169	295	253	248	251	177	145	146
Kentucky	150	185	179	295	298	311	313	401	310	306
Louisiana	656	695	915	1159	1217	1111	1352	1220	1058	904
Maine	67	50	56	77	137	139	80	55	41	42
Maryland	873	1019	1033	1984	2210	2885	2272	2155	1628	1634
Massachusetts	816	942	861	1904	2019	1365	1283	1100	763	1250
Michigan	528	574	847	1540	1074	1056	1031	937	802	714
Minnesota	172	200	238	588	382	406	322	246	176	206
Mississippi	214	261	226	384	412	411	412	447	359	432
Missouri	563	577	706	1621	814	676	846	689	545	492
Montana	16	30	22	26	29	24	30	42	34	18
Nebraska	41	65	61	151	106	112	98	97	75	74
Nevada	170	225	247	536	429	409	449	459	466	257
New Hampshire	57	46	53	89	90	115	99	68	53	47
New Jersey	2233	2419	2192	3409	5199	4712	3970	3742	2484	2061
New Mexico	102	109	108	279	164	229	113	228	220	125
New York	7625	7666	7948	13893	15038	12504	13194	12414	11273	7655
North Carolina	519	527	649	1001	1293	1012	981	857	812	789
North Dakota	2	13	1	10	28	6	10	10	10	6
Ohio	587	595	803	1163	1326	1180	1109	938	792	585
Oklahoma	216	172	240	652	346	269	278	288	298	185
Oregon	276	288	290	658	577	506	500	356	236	198
Pennsylvania	1149	1093	1392	2132	2809	2659	2256	2121	1891	1806
Puerto Rico	1466	1738	1753	2581	2604	2540	2125	2205	2012	1448
Rhode Island	93	76	121	231	273	283	180	160	134	120
South Carolina	364	344	354	1121	1169	984	951	795	772	984
South Dakota	1	9	9	23	17	20	17	9	17	17
Tennessee	306	329	409	851	847	872	895	787	690	769
Texas	2799	3048	3190	6062	5790	5074	4339	4876	4456	3715
Utah	86	108	129	278	136	152	198	157	150	154
Vermont	19	21	22	26	81	31	40	33	21	16
Virgin Islands	7	12	21	47	40	58	33	54	63	33
Virginia	611	646	658	1360	1367	1139	1505	1253	998	912
Washington	693	591	532	1172	1179	921	769	758	523	393
West Virginia	61	52	70	76	78	113	144	110	122	63
Wisconsin	179	195	224	622	399	358	323	251	222	183
Wyoming	7	11	11	32	19	14	13	17	4	8

Source: Charts here and on p. 107 courtesy of the Centers for Disease Control and Prevention, Atlanta.

(Continued from page 106)

how tentative the nation's control is over the epidemic. The studies, which were presented at the XIII International AIDS Conference in Durban, South Africa, include the following:

- The population of 15- to 20-year-old men who have sex with men (MSM) in the United States has experienced a resurgent HIV epidemic.<sup>1</sup>

- Highly active antiretroviral therapy (HAART) fails to fully suppress HIV in nearly two-thirds of patients over a 15-month period. The study's suppression criteria were higher than what is needed to keep patients healthy. However, that also means many patients will have to switch to more complex and expensive regimens to maintain suppression of their viral loads.<sup>2</sup>

### ***Bisexual men engage in more risky behaviors***

- Bisexual males are more likely to engage in risky sexual behavior with men, as well as with women, and are just as likely to have HIV infection. Among MSM, 17% said they recently had sex with both men and women, and 4% had had unprotected sex with both genders. Therefore, bisexual men serve as a bridge for HIV transmission between MSM and women.<sup>3</sup>

- Women are less likely than men to achieve HAART treatment success. In the CDC study, nearly 30% of women failed to show a significant decrease in viral load after initiating treatment.<sup>4</sup>

- African-Americans and women are less likely to be prescribed HAART than are white men. Others who are less likely to be prescribed antiretroviral therapy include people who have a history of psychosis, injection drug use, and alcoholism.<sup>5</sup>

- About 22% of gay and bisexual men ages 15 to 25 have never been tested for HIV, which suggests the need for intervention strategies to increase testing.<sup>6</sup>

- More than one-quarter of women taking HIV medication were unable to adhere completely to their treatment regimen. The factors correlated with poor adherence were depression, HIV-related stress, loss of family income, and family illness.<sup>7</sup>

- HIV-infected gay and bisexual men increasingly are engaging in unprotected anal sex. A

third of MSM surveyed who engaged in anal intercourse within the past year had done so without protection.<sup>8</sup> (See story on increasing risk behaviors, p. 111.)

- For the 25 states that have HIV surveillance data from 1998, the highest rate of African-Americans living with HIV and AIDS was in Jersey City, NJ, and the highest rate of Hispanics living with HIV and AIDS was in Newark, NJ.<sup>9</sup>

- CDC surveillance data estimate the number of people living with AIDS in the United States through June 30, 1999, to be 308,933, with most of the AIDS cases hailing from the states of New York, California, Florida, and Texas. (See CDC charts on people living with AIDS, p. 107, and the number of reported AIDS cases, p. 108.)

The CDC studies back up other research published in recent months, all of which point to a possible reversal in the trend of decreased morbidity and mortality among HIV-infected Americans.

"We've had 90% reductions in both morbidity and mortality since 1996, and those have been sustained," said **Scott Holmberg**, MD, senior epidemiologist with the CDC's Division of HIV/AIDS Prevention.

But that's only the first half of what has happened since HAART was introduced, Holmberg noted. "The second point is that each successive HAART regimen seems to work less and less long, either because of toxicity or virologic failure," he added.

### ***Complex regimens becoming less effective***

Research presented by Holmberg in Durban showed that on average patients stayed on their first HAART regimen less than 11 months before the treatment proves ineffective or intolerable. For patients on the second HAART regimen, suppression lasted about 8.1 months on average, and for patients taking a third HAART regimen, virologic success lasted about 6.4 months on average.<sup>10</sup> The study analyzed medical data from more than 1,600 AIDS patients nationwide.

"What that means is more and more complex and expensive regimens are less and less successful in keeping viral loads suppressed and keeping people alive and healthy," he explained.

“And the implication is that we must develop new drugs and new strategies before we exhaust the therapeutic armory for HIV.”

Holmberg’s study on viral suppression used strict criteria for determining that treatment was a success. The treatment had to produce and maintain one log, a 10-fold or more reduction in viral load, and a constant or increased CD4 cell count. Based on those criteria, the study found that little more than one-third of patients on HAART for at least 15 months had achieved success in suppressing HIV.

“We felt that was clearly a success,” he said. “But the fact is there are many people who had half a log reduction in viral load, and their CD4 cell count went up, and they were successful but weren’t included in our analysis of successful patients.”

Another CDC study looked at the HAART failure rate within the first five months of therapy for women vs. men. Using a small sample of patients taking HAART for the first time, the study found that women were significantly more likely to have a treatment failure. All participants were assessed to be ready to take HAART, to have a support partner to help them adhere to their regimen, and were not currently abusing illegal drugs.

### ***Women more likely to fail HAART***

Nearly 30% of the women failed to show a significant decrease in their viral load after beginning treatment, while only 10% of men failed HAART. Success criteria were at least a two-log drop in viral load or a viral load of fewer than 3000 copies/mL.

“The women who did not show early success tended to be more depressed, reported more stress, had less overall social support, and they had more misconceptions about HAART and how the meds worked,” said **Linda Koenig**, PhD, assistant chief for behavioral science and a clinical psychologist in the Mother-Child Transmission and Pediatric and Adolescent Study Section of the CDC’s Division of HIV/AIDS Prevention Epidemiology Branch.

The women who were early HAART failures tended to have experienced stress in the prior six months that could have included separation

from partner, death of a family member, inability to move when expecting to move, loss of a job, incarceration, or conflict with health care workers.

Koenig said the study shows how important it is to assess new HIV patients for life stresses and other factors before beginning antiretroviral therapy. “Assess them for the need for social services to help them with major life events, for mental health services, particularly in relation to depression, and for education and counseling about HAART,” she advised.

### ***Women less likely to adhere with regimen***

This research, added to another study showing that women are less likely to be prescribed HAART, show that medical providers have to face some important challenges in reaching women with HIV, said **Helene D. Gayle**, MD, MPH, director of the CDC’s National Center for HIV, STD, and TB Prevention.

“Findings presented in Durban show that women are less likely to be prescribed HAART and, for those who are, obstacles such as HIV-related stress and income loss can stand in the way of proper adherence,” Gayle said. “These results point to the reality that these treatments are complex and are a lifelong proposition.”

Health professionals need to recognize that their patients need more than the antiretroviral drugs, she added. “And they must do what they can to make sure their HIV-infected patients are linked to the social and psychological services they need to deal with the reality of living with HIV.”

Another CDC researcher took a close look at what factors prevent an HIV-infected woman from adhering to her medication regimen. The study of 520 HIV-infected women eligible for HAART found that only 288 (55%) of the women were taking any antiretroviral drugs.

“What happens is a lot of women who have been prescribed have not taken the meds,” said **Jan Moore**, PhD, assistant chief in the CDC’s Sexual Transmission and Injection Drug Use Section.

Of the 288 women taking HAART, about 26% were unable to adhere completely to their drug regimen. The women who failed to take their

drugs regularly were more likely to have depressive symptoms, adverse life events, and HIV-related distress. Factors such as recent illicit drug use, viral load, CD4 cell count, and HIV-related symptoms appeared to have no impact on the women's adherence.

"It would be helpful if we were doing more to screen for psychological distress, depression, stress, and a number of other factors," Moore says. "Taking a person's psychological state into account in thinking about how adherent they might be is really important."

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## At-risk men failing to change behavior

*CDC studies prove problem continuing to grow*

New research shows that HIV-infected gay and bisexual men increasingly are having unprotected anal intercourse. Also, not enough young gay men who are at risk for HIV infection are being tested. Together, those trends highlight the continual need for HIV prevention and education messages aimed at men who have sex with men, an AIDS activist says.

"We have a plethora of information on HIV prevention, but is it really speaking to young people in a language they understand?" said **Julio Abreu**, deputy director of government affairs for AIDS Action in Washington, DC. "That's why it needs to continue to be an evolving message that we give about prevention. Think of it as an ad campaign: Coca Cola wouldn't dream of just saying one jingle time and time over."

Concerned about recent outbreaks of sexually transmitted diseases (STDs) among HIV-infected gay and bisexual men, researchers from the Centers for Disease Control and Prevention (CDC) in Atlanta conducted an extensive, three-year survey to assess their sexual behavior. The survey began in January 1995, just before the advent of highly active antiretroviral therapy, and ended in December 1998.

The CDC presented the results of the study at the XIII International AIDS Conference held in Durban, South Africa.

CDC research into risk behaviors of HIV-positive men who have sex with men (MSM) shows that gay and bisexual men were increasing their sexual risk behaviors even before protease

inhibitors and antiretroviral regimens changed the face of AIDS in this country, reported **Paul Denning**, MD, medical epidemiologist with the CDC's Division of HIV/AIDS Prevention.

"A lot of people are attributing all of this risk behavior just to the protease inhibitors and HAART and new treatment regimens," Denning said. "But these trends go back quite a while."

### ***At-risk population no longer careful***

Denning said AIDS is no longer as frightening to people as it was in the early 1980s, when it meant rapid death. By the 1990s, HIV-infected people were living longer, taking AZT and other treatments.

"As early as 1990," he said, "there were reports of a resurgence of unsafe sex in the United States and the Netherlands," Denning said. "Throughout the 1990s, there have been sporadic outbreaks of STDs, so there probably has been a gradual decline in safe sexual behavior."

Denning's research found that HIV-infected MSM, interviewed by CDC investigators in 1997 and 1998, were significantly more likely to have anal intercourse and unprotected anal intercourse than were MSM interviewed in 1995-96.

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"The HIV-infected population is a group we've often ignored in our prevention work. So for clinicians, this is an optimum time to intervene: at the time of diagnosis and at the first intake of the patient."

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In the earlier group, 29% reported having had unprotected anal intercourse, vs. 38% in the 1997-1998 group.<sup>1</sup> Risk factors for MSM having anal intercourse included men who injected drugs, had fewer than 12 years of education, had a steady sex partner of unknown status, and had "\$5 sex partners."<sup>1</sup>

Investigators interviewed 5,094 MSM in 12 cities and states who were newly reported with HIV or AIDS. Of the 1,942 men who met the inclusion criteria, 27% of those who were sexually active had at least one episode of unprotected

anal intercourse in the year before they were interviewed. If they had at least one episode of anal intercourse without condoms, it was considered unprotected anal intercourse. The men who were having sex with one HIV-positive partner were excluded. The increases in unprotected anal intercourse were noted in both MSM participants, Denning said.

This study highlights the importance of focusing HIV prevention messages on members of the HIV-infected MSM population, Denning said. "The HIV-infected population is a group we've often ignored in our prevention work," he added. "So for clinicians, this is an optimum time to intervene, at the time of diagnosis and at the first intake of the patient."

### ***Gay, bisexual men failing to get tested***

However, even this strategy only works when at-risk MSM get tested for HIV. Research by another CDC investigator showed that a large number of young gay and bisexual men have never been tested for HIV.

"I think this reflects a trend that has been seen in a variety of surveillance studies of men who have sex with men," said **Esther Sumartojo**, PhD, team leader for the Community Intervention Research Team in the CDC Division of HIV/AIDS Prevention.

Sumartojo's study showed that among young MSM, 22% reported they had never been tested for HIV. Of those who had been tested, 1.5% were HIV-positive, 95% were HIV-negative, and 3% didn't know their test results.<sup>2</sup>

CDC investigators interviewed 2,621 MSM, ages 15 to 25, in 10 cities. They chose venues known to be frequented by young MSM, including gay bars, dance clubs, coffee houses, parks, and bookstores. Investigators conducted 20 minute on-the-site interviews with the eligible men.

They found that African-American men were more likely to report being tested than any other race, and men with less education were less likely to report being tested.<sup>2</sup>

"We asked the men if they could name a comfortable place to be tested," Sumartojo explained. "To me, that was one of the interesting things about this study, because whether or not they could name a comfortable place had a strong

association to whether they had ever been tested.”

Sumartojo and other researchers are continuing to analyze the data and will publish a study later that looks what kinds of settings MSM consider “comfortable” for HIV testing.

For HIV prevention to succeed in the future, the nation will need to continue providing highly targeted HIV prevention programs directed toward high-risk people and people who have already become infected, said **Helene D. Gayle**, MD, MPH, director of the CDC’s National Center for HIV, STD, and TB Prevention.

“We must increase the number of people who know their HIV status and link HIV-infected individuals not only to the treatment they need, but also to prevention services, including substance abuse treatment and mental health services, to support them in establishing and maintaining safer behaviors over a lifetime,” Gayle said.

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## Increasing HIV rate result of several factors

*Goal is to cut infections in half by 2005*

[AIDS Alert asked **Ronald O. Valdiserri**, MD, deputy director of the National Center for HIV, STD, and TB Prevention at the Centers for Disease Control and Prevention (CDC) in Atlanta, to discuss the significance of some of the CDC’s HIV research presented at the XIII International AIDS Conference, held in July in Durban, South Africa. Here are his answers:]

**AIDS Alert:** CDC research now demonstrates how well HIV prevention efforts work among the highest-risk populations in the United States. So why are we beginning to see a resurgence of HIV risk behavior among gay men, and what can be done about this problem?

**Valdiserri:** There most likely is no single factor contributing to the increases in risk behavior we are seeing among gay men, but rather a complex combination of factors, including fatigue with safer sex messages and the misperception that HIV is no longer a serious disease with the availability of more effective treatments. Private funding for HIV prevention programs has been drastically cut as donations to AIDS-related community-based organizations have dropped off.

In addition, throughout the last decade, the need for HIV prevention has expanded to multiple populations, yet public funding for prevention has remained fairly flat compared to increases for treatment and research. Therefore, many HIV prevention programs have not been sustained in recent years. HIV prevention aimed at gay men must be comprehensive and sustained for each new generation.

**AIDS Alert:** In the past couple of years, the CDC and Clinton administration have focused more effort and funds on targeting prevention programs for African-Americans, Latinos, and women. Do you believe these efforts will be enough to stop the high incidence of HIV among these groups, and, if so, when do you think we’ll begin to see a drop in their HIV infection rates?

**Valdiserri:** HIV prevention needs are greater today than ever before in terms of the expanding diversity of people affected and the increasing number of people living with HIV. With resources for prevention being stretched further and further, it is difficult to predict when we may see declines in HIV infections in any group at risk. CDC has long recognized the disproportionate impact of the epidemic on communities of color and has been working with community-based organizations since the 1980s to provide HIV prevention services in African-American and Latino communities. Recent supplemental and emergency funds

from Congress have enabled us to take an important step in building capacity in communities of color to address gaps in HIV prevention infrastructure and other critical needs in these communities. However, we still have a long way to go if we are going to achieve our goal of reducing the number of annual HIV infections by half by 2005. Reaching this goal will require an increased commitment from both the public and private sectors.

**AIDS Alert:** Do you believe it is possible that we'll ever see the HIV rates of infection among women and minorities fall to pre-1990 levels, despite the problem of injection drug use and the fact that the current Congress is solidly against any needle exchange programs? If so, why, and if not, what's the best we can hope for?

**Valdiserri:** I do think it is possible to make tremendous strides in reducing the number of new infections in all groups at risk for HIV infection, given adequate will and resources to do so, continued collaboration with the communities affected, and the ability to implement effective strategies. Some of our greatest prevention successes have been among injection drug users where programs have been applied that include access to sterile injection equipment, substance abuse treatment, prevention case management, and other basic prevention strategies.

Needle exchange programs have proven an effective aspect of these efforts but are clearly not the only intervention needed. Substance abuse treatment programs are crucial — not only for injection drug users, but for all HIV-infected individuals who have a substance abuse problem.

**AIDS Alert:** Does the CDC have any plans to target prevention efforts to the bisexual male population, which your research shows to be an important “bridge” for HIV transmission to women? How would a prevention program aimed at this population work?

**Valdiserri:** We are currently providing prevention outreach to bisexual men through a number of initiatives. Most recently, we funded several organizations serving gay and bisexual men of color, a population where a significant percentage of men who have sex with men actually identify

themselves as heterosexual. A key factor to reaching these individuals is to provide information in a way that does not require a man to self-identify as “gay” or “bisexual” in order to obtain HIV prevention services.

For example, we fund a program in St. Louis that organizes an annual blues festival that provides HIV prevention information to African-American men who have sex with men but may not self-identify as “gay” or “bisexual.” The festival does not advertise or identify as an HIV/AIDS event but provides HIV workshops, makes HIV counseling and testing available, and distributes condoms and HIV prevention literature alongside the entertainment events and cultural programs. Additionally, at a community level, we continue to work to address the stigma that prevents these men from accessing the services they need.

**AIDS Alert:** How can health officials and the CDC solve the problem of young gay men and other at-risk people not being tested for HIV? Do you think the rapid HIV test, introduced at the recent international AIDS conference, will help improve the testing rate of at-risk groups?

**Valdiserri:** Certainly, advances in technology that make HIV testing more accessible and acceptable are critical for HIV prevention. Approval of new rapid tests in the U.S. could be one of the most important HIV prevention milestones in this decade. Of the estimated 800,000 to 900,000 people currently living with HIV infection in the United States, one-third do not know they are infected. Studies have shown that, in addition to receiving the benefits of early HIV treatment, infected individuals who learn their HIV serostatus adopt safer sex behaviors, which can help prevent the further spread of the epidemic.

CDC is moving forward with a major initiative to increase the number of HIV-infected individuals who know their HIV serostatus. Additionally, we are funding several communities to evaluate innovative approaches to testing. However, it is important to remember that HIV testing is only one element of a comprehensive approach to HIV prevention, which should also include components such as outreach, peer education, and comprehensive school health education. ■

## New rapid HIV test accurate, easy to use

*U.S. Army studies it for potential use in military*

The long wait for a rapid HIV test may be over early next year, as the manufacturer of one of the more promising tests being researched moves forward with studies at 20 U.S. sites.

The OraQuick HIV-1/2 rapid HIV test, manufactured by Epitepe Inc. of Beaverton, OR, was introduced at the XIII International AIDS Conference in Durban, South Africa. It collects oral fluid in 15 seconds, presents test results in 20 minutes or less, requires no needles, is simple to use, and has demonstrated an accuracy of more than 99%.

"Its sensitivity is 100%; its specificity is greater than 99.5%, and it is very easy to use since it works on serum, plasma, or saliva, and it requires no reagents to be added, and all material are included in the kit," said Lt. **Hassan Zahwa**, MS, manager of the HIV Diagnostic Laboratory at Walter Reed Army Institute of Research in Rockville, MD.

### *Test still being evaluated*

Walter Reed Army Institute has tested a variety of rapid HIV tests, including some that have been as sensitive as OraQuick and others that have had a sensitivity level as low as 66%, Zahwa said.

So far, the OraQuick device has been evaluated in 100 samples. The next step will be to evaluate it in 1,000 samples and then on 12,000 samples. Rapid HIV tests that continue to prove highly accurate at the 12,000-sample level are possible candidates for use by the U.S. Army and in military hospitals, he said. "OraQuick is one of the tests we're very excited about," he added.

Epitepe received approval in April for its investigational device exemption from the Food and Drug Administration (FDA) in Washington, DC, and has begun testing about 7,000 samples as part of the data needed to support an application for FDA approval. The company plans to file a pre-market approval application in January 2001 for HIV-1 and HIV-2 screening using OraQuick.

The test works as easily as over-the-counter pregnancy tests: A person swabs his or her upper

and lower outer gum with the flat pad end of the device. Then the device is placed into a vial containing a developer solution. Within 20 minutes, a colored line appears in the control area to show that the test was run properly. If the person is HIV

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**AMERICAN HEALTH  
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## Special Issue: XIII International AIDS Conference

positive, a second line appears in the test area.

Safe and accurate rapid HIV testing needs to be approved quickly by the FDA so AIDS service organizations (ASOs) and others can begin to reach some of the estimated 300,000 Americans who are HIV positive and don't know it, said **Julio Abreu**, deputy director of government affairs for AIDS Action of Washington, DC.

"In some cases, more than 25% of people who are tested never come back to get their results," he said, "so if you could give a test result to a person in 10 to 20 minutes, that would really capture the folks who otherwise would be lost."

ASOs could offer the rapid test along with counseling and HIV education in a variety of settings, including needle exchange vans, he said. "Then we'll begin to make a dent on that 300,000 people who are positive and don't know it."

### *Army could use rapid test in the field*

The U.S. Army needs FDA-approved rapid HIV tests for two reasons, Zahwa said. First, the test would be used to assess prophylaxis administration in the event a health care worker or other Army person is accidentally exposed to the virus.

"Depending on the result of these tests, the physician can make a decision about administering prophylaxis," he said. "We've also thought about using it to diagnose HIV in the field or in foreign countries when our soldiers are exposed and the HIV status of the sources is to be determined."

Second, physicians in military hospitals could use the test to check a pregnant woman's HIV status. If a pregnant servicewoman had not previously sought prenatal care or had not been tested for HIV, the rapid test could let her doctors know whether they needed to administer quick doses of AZT or nevirapine to reduce her risk of spreading HIV to her baby during the delivery.

Physicians would make the decision of whether to use the test under those circumstances, but the Army could provide them with data and literature supporting the test's reliability, Zahwa said.

The military will not have as much use for the test in determining the HIV status of enlisted men and women, because that is done routinely every two years by mass screening with FDA-approved ELISA and Western blot tests, he said. However, the HIV test might be used by most civilian HIV testing and treatment clinics, he said. ■

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## 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. ■

# Common Sense About

# AIDS®

## HIV definitely causes AIDS, and here's why

*Government medical experts tell truth about various myths*

**I**t would be difficult to ignore the occasional rumors and myths that surface about HIV and AIDS. Even some national leaders have expressed skepticism about whether the human immunodeficiency virus (HIV) actually does cause AIDS.

Earlier this year, for example, South African President **Thabo Mbeki** was widely criticized for saying he was interested in hearing more about how HIV might not be the cause of AIDS. But thousands of scientists and researchers around the world say HIV does cause AIDS, and nearly 20 years of research proves that to be true.

In the summer of 2000, more than 5,000 scientists from around the world signed the Durban Declaration, which states that HIV causes AIDS.

The National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, MD, has prepared some answers to the myths about HIV and AIDS. Here's what the NIAID says:

**Myth:** HIV antibody testing is unreliable.

**Fact:** Diagnosis of infection

using antibody testing is one of the best-established concepts in medicine. HIV antibody tests exceed the performance of most other infectious disease tests in both sensitivity (the ability of the screening test to give a positive finding when the person testing truly has the disease) and specificity (the ability of the test to give a negative finding when subjects tested are free of the disease under study). Current HIV antibody tests have sensitivity and specificity in excess of 98% and are therefore extremely reliable.

**Myth:** There is no AIDS in Africa. AIDS is nothing more than a new name for old diseases.

**Fact:** The diseases that have come to be associated with AIDS in Africa — such as wasting syndrome, diarrheal diseases, and TB — have long been severe burdens there. However, high rates of mortality from those diseases, formerly confined to the elderly and malnourished, are now common among HIV-infected young and middle-aged people.

**Myth:** HIV cannot be the cause of AIDS because researchers are unable to explain precisely how HIV destroys the immune system.

**Fact:** A great deal is known about the pathogenesis of HIV disease, even though important details remain to be elucidated. However, a complete understanding of the pathogenesis of a disease is not a prerequisite to knowing its cause. Most infectious agents have been associated with the diseases they cause long before their pathogenic mechanisms have been discovered.

Because research in pathogenesis is difficult when precise animal models are not available, the disease-causing mechanisms in many diseases, including tuberculosis and hepatitis B, are poorly understood. The critics' reasoning would lead to the conclusion that *M. tuberculosis* is not the cause of tuberculosis or that hepatitis B is not a cause of liver disease.

**Myth:** AZT and other antiretroviral drugs, not HIV, cause AIDS.

**Fact:** The vast majority of people with AIDS never received antiretroviral drugs, including those in developed countries prior to the licensure of AZT in 1987.

As with medications for any serious diseases, antiretroviral drugs can have toxic side effects. However, there is no evidence that antiretroviral drugs cause the severe immunosuppression that typifies AIDS, and abundant evidence that antiretroviral therapy, when used according to established guidelines, can improve the length and quality of life of HIV-infected individuals.

In the 1980s, clinical trials enrolling patients with AIDS found that AZT given as single-drug therapy conferred a modest and short-lived survival advantage compared to placebo. Among HIV-infected patients who had not yet developed AIDS, placebo-controlled trials found that AZT given as single-drug therapy delayed, for a year or two, the onset of AIDS-related illnesses. Significantly, long-term follow-up of these trials did not show a prolonged benefit of AZT, but also never indicated that the drug increased disease progression or mortality. The lack of excess AIDS cases and death in the AZT arms of those placebo-controlled trials effectively counters the argument that AZT causes AIDS.

**Myth:** Behavioral factors such as recreational drug use and multiple sexual partners account for AIDS.

**Fact:** The proposed behavioral causes of AIDS, such as multiple sexual partners and

long-term recreational drug use, have existed for many years. The epidemic of AIDS, characterized by the occurrence of formerly rare opportunistic infections such as *Pneumocystis carinii* pneumonia (PCP) did not occur in the United States until a previously unknown human retrovirus — HIV — spread throughout certain communities.

Compelling evidence against the hypothesis that behavioral factors cause AIDS comes from recent studies that have followed cohorts of homosexual men for long periods of time and found that only HIV-seropositive men develop AIDS.

Other studies show that among homosexual men and injection-drug users, the specific immune deficit that leads to AIDS — a progressive and sustained loss of CD4+ T cells — is extremely rare in the absence of other immunosuppressive conditions. For example, in the Multicenter AIDS Cohort Study, more than 22,000 T-cell determinations in 2,713 HIV-seronegative homosexual men revealed only one individual with a CD4+ T-cell count persistently lower than 300 cells/mm<sup>3</sup> of blood, and that individual was receiving immunosuppressive therapy.

**Myth:** *The distribution of AIDS cases casts doubt on HIV as the cause. Viruses are not gender-specific, yet only a small proportion of AIDS cases are among women.*

**Fact:** The distribution of AIDS cases, whether in the United States or elsewhere in the world, invariably mirrors the prevalence of HIV in a

population. In the United States, HIV first appeared in populations of homosexual men and injection-drug users, a majority of whom are male. Because HIV is spread primarily through sex or by the exchange of HIV-contaminated needles during injection-drug use, it is not surprising that a majority of U.S. AIDS cases have occurred in men.

Increasingly, however, women in the United States are becoming HIV-infected, usually through the exchange of HIV-contaminated needles or sex with an HIV-infected male. The CDC estimates that 30% of new HIV infections in the United States in 1998 were in women. As the number of HIV-infected women has risen, so too has the number of female AIDS patients in the United States. Approximately 23% of U.S. adult/adolescent AIDS cases reported to the CDC in 1998 were among women. In 1998, AIDS was the fifth leading cause of death among women ages 25 to 44 in the United States, and the third leading cause of death among African-American women in that age group.

In Africa, HIV was first recognized in sexually active heterosexuals, and AIDS cases in Africa have occurred at least as frequently in women as in men. Overall, the worldwide distribution of HIV infection and AIDS between men and women is approximately 1 to 1.

*[For reference information and more information on the myths about HIV and AIDS, visit the NIAID's Web site at [www.niaid.nih.gov/spotlight/hiv00/default.htm](http://www.niaid.nih.gov/spotlight/hiv00/default.htm).]* ■