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Stem cell
distribution

HIV TRANSMISSION

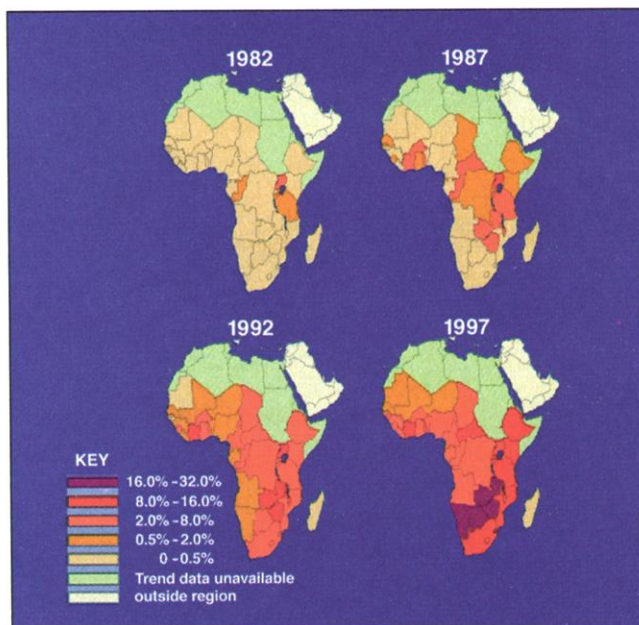
AIDS Researchers Look to Africa for New Insights

SAN FRANCISCO, CALIFORNIA—A remarkable shift in emphasis occurred here last week at the largest annual AIDS meeting* held in the United States. Instead of reports from North America and Europe once again dominating the meeting, many of the most significant findings came from Africa, where 70% of the world's 33 million HIV-infected people live. As HIV infection rates have plateaued in most developed countries, investigators are increasingly turning to Africa, where the epidemic is still exploding. "When it moves that rapidly, there are many things you can do about it," explains Anthony Fauci, head of the U.S. National Institute of Allergy and Infectious Diseases (NIAID).

As the geographic focus shifts, so do the research questions. In North America and Europe, investigations center on elucidating the relationship between HIV and the immune system and also determining how best to use the 14 marketed anti-HIV drugs. But in sub-Saharan Africa, where infection rates among adults have climbed to 25% in some countries, such questions have little relevance, as only the elite can afford anti-HIV drugs. The main issue, instead, is how to stop transmission of the virus. As several reports at the meeting emphasized, the situation may be more complicated than previously assumed.

One puzzling question is why HIV infection rates are so much higher in some African populations than in others. To find out, Anne Buvé, an epidemiologist at the Institute of Tropical Medicine in Antwerp, Belgium, launched a huge study in four countries that compared sexual habits, male circumcision practices, and rates of infection with various sexually transmitted diseases (STDs). Buvé's international research team randomly selected approximately 1000

men and 1000 women from four towns: Cotonou, Benin; Yaoundé, Cameroon; Kisumu, Kenya; and Ndola, Zambia. HIV prevalence in Cotonou and Yaoundé ranged from 3.3% to 7.8%; in Kisumu and Ndola, it ranged from 19.8% to a whopping 31.9%.



Epidemic disaster. The percentage of adults (ages 15 to 49) in Africa infected with HIV has skyrocketed.

To their surprise, the researchers found little connection between HIV prevalence and the lifetime number of sexual partners, contact with sex workers, condom use with sex workers, or the age at which a person first has sex. "We believe that any differences in sexual behavior were probably outweighed by differences in efficiency of HIV transmission during sexual intercourse," said Buvé. Two clues about transmission factors emerged that led Buvé and colleagues to this conclusion. The two cities that had the highest HIV prevalence also had the lowest rate of male circumcision and the highest rate of infection with ulcerative STDs, such as herpes simplex virus type 2 and *Trichomonas vaginalis*.

Buvé's study is "probably the clearest

demonstration ... that differences in HIV prevalence are not simply due to behavior," said epidemiologist Kevin DeCock of the U.S. Centers for Disease Control and Prevention. The data, if borne out, might well force a rethinking of prevention campaigns that solely emphasize behavior change, without also screening for STDs, distributing condoms, and even encouraging male circumcision.

Work by Ruth Nduati of the University of Nairobi in Kenya highlighted how difficult it is to transfer gains made in wealthy countries to poorer settings. One of the crowning achievements in AIDS prevention to date was

a 1994 study showing that the anti-HIV drug AZT can block transmission of the virus from an infected mother to her newborn. As Nduati noted, in 1997, the United States recorded just 500 cases of mother-to-child transmission of HIV. But that same year, 600,000 other babies—90% of them in sub-Saharan Africa—became infected by their mothers, the vast majority of whom could not afford the drugs. Today, a \$4 treatment can significantly reduce mother-to-child transmission at birth, but as Nduati noted, even that treatment, if they can afford it, may not help many poor women in Kenya.

Although several studies have shown that breast-feeding can transmit HIV, the Kenyan study is the first to evaluate whether using formula can affect transmission rates. As expected, about 20% of the babies in the study became infected before or at birth. Nduati

and co-workers from the University of Washington went on to look at the uninfected babies, comparing 197 breast-fed babies to 204 who received formula. They found that an additional 16.2% of the breast-fed group became infected later, most (75%) during the first 6 months of life. "The results of this study have significant public health implications," concluded Nduati. "Breast milk avoidance could potentially decrease mother-to-child transmission by 44%," a reduction similar to that achieved with a short course of AZT or other anti-HIV drugs.

But this doesn't necessarily mean that formula-feeding would save lives. In many parts of Africa where water supplies are contaminated, switching to formula is likely to increase mortality from intestinal diseases.

CREDIT: JOINT UNITED NATIONS PROGRAMME ON HIV/AIDS (UNAIDS)

* 7th Conference on Retroviruses and Opportunistic Infections, 30 January to 2 February.

Hints of
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plasmaClinton's final
budgetMonkey
shortage hits
AIDS research

The cost of formula is also a serious barrier, especially in Kenya, which taxes formula so heavily that a 1-month supply costs \$1000.

Many AIDS researchers believe that the best hope of thwarting HIV lies in the development of a vaccine. But Oxford University's Rupert Kaul presented some unexpected findings from another study in Kenya that suggest researchers may need to rethink some fundamental precepts about what might constitute a working vaccine.

Kaul collaborated with investigators from the University of Kenya and the University of Manitoba who have been studying a group of Kenyan sex workers since 1984. About 15% of the 1900 women have remained uninfected by HIV, despite having an average of five clients per day and as many as 70 unprotected exposures to the virus each year. But Kaul reported that 10 of these women who took a 2-month break from sex work became infected when they returned. Kaul stressed that it's "not unexpected" that some of these women would become infected, noting that the 3-year cut-off they use to define someone as exposed but uninfected is "purely arbitrary." What is odd, though, is that they became infected after taking a break from high-risk sex. "That's the most fascinating thing I've heard in months," said NIAID's Fauci.

While fascinating, the findings are nonetheless difficult to interpret. One possible explanation is that repeated exposure to the virus is needed to maintain whatever immunological barrier is protecting the women. If so, a vaccine may need to be given repeatedly. Another possibility under investigation is that these women developed antibodies to the foreign, or "allo," white blood cells in semen. Because HIV also has pieces of human white blood cells on its surface, which the virus picks up from every cell it infects, these alloantibodies might block the virus from infecting the women's cells. Perhaps when the women stopped sex work, these antibody levels fell, rendering the women more vulnerable to HIV.

The research tilt toward Africa and other developing regions will surely intensify during the next year, and not only because that's where HIV is hitting the hardest. This summer, some 10,000 AIDS researchers are expected to travel to Durban, South Africa, for the 13th World AIDS conference, which, in another sign of the times, will be the first one held in a developing country.

—JON COHEN

SCIENTIFIC ADVICE

Academies Get Together To Tackle the Big Issues

BERN, SWITZERLAND—While heads of state and business leaders were capturing the headlines at last week's World Economic Forum in snowy Davos, an unheralded group of science academy leaders quietly gathered behind the scenes. Their goal: to take some crucial steps toward creating a new mechanism for providing impartial scientific advice to international organizations.

The proposed new body, tentatively called the InterAcademy Council (IAC), would in some ways be an international version of the U.S. National Research Council, which sets up scientific committees to advise the U.S. government. Similarly, the United Nations or World Bank could ask the IAC to appoint international panels of leading researchers to address global issues such as the effect of genetically modified plants on agriculture, the threat of emerging infectious diseases, how to protect threatened ecosystems, and how to bridge the information divide between the world's rich and poor.

Participants in last week's meetings in Davos and Zurich—which included the presidents of a dozen of the world's national science academies and several other officials—told *Science* that such a global science advisory body could be approved by mid-May. "We easily reached a general agreement on a plan after spending about 20 hours together," says biochemist Bruce Alberts, president of the U.S. National Academy of Sciences, who had proposed such an international body last spring.

While the Davos participants agreed on the general outlines of the IAC, Alberts says remaining details will be hammered out by a working group of academy presidents or their equivalents from France, India, Germany, and Brazil. That group will make its recommendations in Tokyo in May to the steering committee of the InterAcademy Panel on International Issues (IAP), a loose association of about 80 national science academies that holds conferences and issues statements on issues of common interest.

F. Sherwood Rowland, a U.S. Nobel laureate who co-chairs the IAP and helped set it up in 1995, sees no "major stumbling blocks" in convincing the IAP to agree to the proposed new IAC. But Rowland, who attended the Davos meetings, says some issues remain to be resolved. They include avoiding duplication of effort among the planned IAC, the InterAcademy Panel itself, and the International Council for Science (ICSU), a Paris-based organization of scientific unions and national academies.

At any given time, the IAC would be comprised of representatives from 15 academies. Some larger academies, such as those of the United States, Russia, China, Japan, India, Brazil, and several European countries, would likely be selected for long-term—possibly 10-year—appointments on the council, while smaller academies would be appointed for 3-year terms initially. In general, the intention is to rotate the IAC membership



Internationalizing. NAS president Bruce Alberts.

among the 80 or so national science academies that are presently members of the InterAcademy Panel. The council would carry out such functions as naming the expert committees and approving the scope of studies requested by outside organizations. The IAC would have a small permanent secretariat, probably based in a European nation, such as Sweden or Switzerland, with good Third World rapport. "The procedure would be to first study the problems posed to see whether the IAC can form a well-balanced study group ... and then run most of the work via the Internet," said the French academy's president, chemist Guy Ourisson. The goal is for any studies to be turned around relatively quickly, ideally within a few months.

Sudanese mathematician Mohamed Hassan, president of the African Academy of Sciences and executive director of the Third World Academy of Sciences, strongly favors the IAC concept, but he wants to make sure that "the developing world—where most countries either don't have academies or have weak ones—has an adequate level of representation." Biochemist Wieland Gevers, president of South Africa's academy, says he hopes the formation of the IAC will spur smaller academies "to take more active