Mumbai Meeting Surveys AIDS in India

For three days last December, over 500 Indian and international scientists, health professionals, government planners, and nongovernmental organizations (NGOs) gathered in Mumbai [Bombay], India, for the International Conference on HIV/AIDS. [Ed. note: the conference was organized by the Institute for Research in Reproduction, the Indian Society for the Study of Reproduction and Fertility, and the University of California at Irvine.] The broad mix of people was mirrored in the meeting's agenda, which ranged from the biomedical front—including treatments and vaccines—to the battle to reduce gender inequality, poverty, and other barriers that limit the use of existing and potential technologies.

In a keynote address, Geeta Rao Gupta, President of the International Center for Research on Women, borrowed from Charles Dickens to describe the HIV/AIDS situation today as "the best of times and the worst of times." On one hand, "we have therapies and treatments today to substantially improve the quality of life of those living with HIV and AIDS," she said. "We have political will in some quarters. We have prevention strategies that work. We have a greater number of supporters and more resources." On the other hand, "the rates of infection in some cities in sub-Saharan Africa and in some populations such as sex workers in India range from 20-30%, exceeding our worst nightmares." Today the promise of biomedical innovations is being eroded by scant resources, social inequality, and stigma, and "it is this that makes these the worst of times."

Sameera Khan

India and HIV/AIDS

P.L. Joshi, Additional Director at India's National AIDS Control Organisation (NACO), the country's lead agency for HIV/AIDS, gave an epidemiological overview of HIV/AIDS in India. Although overall prevalence is still low, India has the second largest population of HIV positive people in the world (after South Africa), estimated at 3.9 million at the end of 2000. The vast majority of cases are due to sexual transmission, but there also are significant numbers of infections through injecting drug use (5%), contaminated blood (4%), and, increasingly, perinatal transmission (2%). Though about 75% of HIV positive people are male, an increasing number of Indian women are now being infected—as seen in the growing prevalence rates among pregnant women at antenatal [prenatal] clinics, which exceed 1% in several states, portending a much wider general epidemic (see the NACO website at www.naco.nic.in).

Interventions and the National Response

Joshi went on to outline NACO's priorities in mobilizing a national response through establishment of a basic prevention and care infrastructure. These include enhancement of India's voluntary testing and counseling (VTC) centers and programs for preventing mother-to-child transmission, much of which should be in place by the end of 2002. Other goals include expanded provision of low-cost care (such as for opportunistic infections), home- and community-based services, research on prevention of mother-to-child transmission (PMTCT), and vaccines and indigenous medicines. NACO is not prioritizing antiretroviral (ARV) delivery for now, although doctors at a handful of clinics around the country are looking at strategies to provide them beyond a small group of affluent private patients.

Finding ways to deliver effective PMTCT programs is another high priority, said Joshi. After completing an 11-center study of an AZT regimen, clinicians are now assessing the feasibility and acceptability of a single-dose nevirapine [Viramune] treatment. Deployment beyond pilot programs will be phased in over the coming year, starting with medical colleges in high-prevalence states, followed by state district hospitals, and moving to states with lower prevalence rates.

But scaling up a comprehensive package of MTCT interventions will be challenging, said R.R. Gangakhedkar of the National AIDS Research Institute (NARI) in Pune. "About 27 million pregnancies annually take place in India, with 40% of women choosing home delivery and another third delivering in private hospitals," he said. So the first challenge is bringing pregnant women into contact with the health-care system. Another challenge is preventing breast milk transmission. As in many African countries, there is ongoing discussion about the feasibility of bottle- versus breast-feeding in settings where lack of clean water, cultural pressures to breast-feed, and other issues complicate feeding decisions (see "AIDS Transmission via Breast-feeding," *IAVI Report*, July/September 2001).

Women, AIDS, and Vaccines

In a rousing plenary presentation Gupta turned the spotlight on the interplay of poverty, vulnerability, gender, and stigma, and on how this could apply to vaccines. "Most of the world's poor are women, and most of the world's women are poor," she began. An AIDS vaccine would offer the ultimate female-controlled prevention, since getting vaccinated without a male partner's consent is far easier than using condoms or even, potentially, microbicides with an uncooperative partner.

But several barriers could limit women's use of vaccines. Chief among them is the possibility that vaccination (or trial participation) could be seen as an admission of risky behavior—a significant barrier to adolescent girls and married women. Gupta emphasized the need for community-based research grounded in local realities, customs, and culture. This means engaging and supporting women's groups, educating community health providers, and planning to offer vaccines within a broad health-care context rather than in stand-alone settings.

Vaccines for India

Bonnie Mathieson of the U.S. Office of AIDS Research began the scientific session on vaccine development by reviewing candidates just entering, or poised to enter, clinical trials, such as GlaxoSmithKline's protein-based vaccine and the DNA/MVA approach being developed by Harriet Robinson's group (see "AIDS Vaccines 2001: Meeting Briefs," *IAVI Report*, October/December 2001). Looking to the future, Mathieson underscored the need to start planning now for Phase III trials in high-risk, hard-to-reach populations.

Two speakers presented approaches involving Indian collaborations. Vijay Mehra, lead scientist for the International AIDS Vaccine Initiative's (IAVI) India program described the three-way partnership with IAVI, India's Ministry of Health and Family Welfare (through the Indian Council of Medical Research), and Therion Biologics (Cambridge, Massachusetts). The joint project is developing an MVA [Ed. note: a pox virus] vaccine incorporating six HIV genes (*env, pol, gag, rev, nef,* and *tat*) from an Indian subtype C consensus sequence, which should enter clinical testing in India starting in 2003. Mehra also outlined other aspects of the partnership, including capacity-building for clinical trials, transfer of manufacturing technology to India, and HIV/AIDS education and advocacy projects.

Rama Amara of Emory University in Atlanta, Georgia, who works with Robinson on DNA/MVA vaccines, presented

a summary of data on monkey challenge studies of this strategy, which should soon enter clinical trials in the U.S. He also reported that clade C versions of the vaccines will be made through a collaboration with the Indian government's Department of Biotechnology.

Vaccine Trials, Ethics, and Communities

In a panel session later the same day, discussants examined the social, ethical, and logistical aspects of conducting AIDS vaccine trials. This is a topic that touches on many sensitivities in India, which has an uneasy history of clinical trials—particularly contraceptive studies—conducted on poor, illiterate communities without proper informed consent.

Quarraisha Abdool Karim of the University of Natal reported on activities in Hlabisa, South Africa, a remote, rural community where almost one in every three adults is HIV positive. Hlabisa began preparing for vaccine trials back in the mid-1990s, picking up momentum in 1997 when it became part of the U.S.-sponsored HIV vaccine trial network (then called HIVNET, now the HIV Vaccine Trials Network [HVTN]).

Initially this meant producing a detailed map and census of households in the area, which has no formal system of addresses. With that infrastructure, community workers began a house-by-house survey of consenting people, collecting information such as basic demographic data, risk behaviors for HIV, and HIV infection rates (which involved providing HIV testing, and pre- and post-test counseling). The researchers also strived to understand the community decision-making process through extensive consultation with community leaders, and have helped form and nurture a community advisory board. "It is about good science being backed by good ethics and community participation," Karim said.

Punnee Pitisuttithum of the Bangkok Vaccine Evaluation Group (BVEG) also stressed the importance of starting preparedness early. BVEG is conducting the Phase III trial of VaxGen's gp120 vaccine in a cohort of 2,545 intravenous drug users (IDUs)—one of two ongoing AIDS vaccine efficacy trials worldwide. Preparations for the trial took years, starting with the establishment of HIV negative IDU cohorts at 16 methadone clinics. Cohort members were followed and given HIV/AIDS prevention counseling for four years, allowing investigators to gather data on the rate and subtype of new HIV infections, key risk factors, and willingness to participate in vaccine trials.

Moving from the preparedness phase to the actual Phase III trial proved fairly smooth, Punnee said. "Our concern was whether volunteers really understood the implications of participating in a clinical trial before enrolling in it. They had to pass two comprehension tests so we could precisely judge this before we enrolled them."

IAVI Report, January/February 2002

HIV Seroprevalence in India*

Group	Place	Prevalence (%)
HIGH RISK		
CSWs	Tamil Nadu	58
	Mumbai	71
IDUs	New Delhi	45
	Imphal (Manipur)	48.8
	Churachandpur (Manipur)	68.4
Truck drivers	Tamil Nadu	9 (1997)
STI patients	New Delhi	<1
	Tamil Nadu	16
	Mumbai	14–16
	Bangalore	16.8
LOW RISK		
Pregnant women	New Delhi	0.3
	Mumbai	2.6
	Tuensang (Nagaland)	4.9
	Churachandpur (Manipur)	5.3
	Tamil Nadu	6.5

**Data are current through 1999*

Sources:
- UNAIDS. Epidemiological Fact Sheets on HIV/AIDS: India, 2000 Update (Revised)
- U.S. Census Bureau. HIV/AIDS Surveillance Data Base. HIV/AIDS Profile: India, June 2000
- World Bank. India HIV/AIDS Update, 2001

***CSW**=commercial sex worker*
***IDU**=injection drug user*
***STI**=sexually transmitted infection*

The questions and discussions that followed the presentations suggested that it was heartening for Indian NGOs to hear about ethical clinical trials being devised in South Africa and Thailand. "If NGO concerns on transparency, full information, and accountability are addressed, we might be able to proceed towards vaccine trials more smoothly," said well-known Indian AIDS activist Ashok Row Kavi of the Humsafar Trust, which works primarily on issues related to men who have sex with men.

Vaccine Testing in India: Hopes and Fears

Turning to perceptions in India, Hema Viswanathan of Probe Qualitative Research (PQR), an Indian market research agency, reported on a small survey she carried out through the IAVI-India partnership. In the study 24 people, most of them leaders of key HIV/AIDS development agencies

and NGOs in Mumbai, Delhi, or Chennai [Madras], were questioned in depth about their attitudes towards AIDS vaccine trials. None of the respondents had prior experience with such trials.

On the whole, the respondents' attitude was one of cautious acceptance. Acceptance was predicated on a number of caveats, such as:

- that the trials be carried out with, and through, the Indian government and other Indian partners;
- that there is extensive expert review at each stage of the trials, including ethical review;
- that trials are run in an open and transparent manner;
- that stakeholders, communities, and the public are kept well-informed;
- that trials test vaccines that would be relevant and available to India.

Respondents' key concerns arose from scenarios in which these conditions are not met, for example, that Indians could be used as guinea pigs in studies that would help only prosperous people in wealthy countries. (On the contrary, India plans to test vaccines based on local strains and targeted for Indian use.) There also were fears that people from already marginalized high-risk groups could be exploited, and that India was being "chosen" for vaccine trials because they could be run less expensively there than elsewhere.

Viswanathan also remarked on the dynamics of the interviews, noting that most respondents moved from an initial acceptance of the idea of trials to a realization, as the detailed questioning progressed, of the complexities involved. As understanding increased, so did the sense of unease and rejection. Finally, participants came to a stage of cautious acceptance, with the caveats noted above. She also said that, if this type of dynamic is seen on a broader public scale once a trial is officially announced, "there might be an easygoing acceptance at the outset, but this could be misleading. It would be important to not take that at face value or expect a smooth passage."

In the next phase of the work, Viswanathan and other IAVI-India partners are conducting a series of focus groups among members of affected communities and meeting with other stakeholders to probe their attitudes and concerns.

The HIV-TB Association

Tuberculosis (TB) is the most common opportunistic infection associated with HIV in India, and several speakers presented data showing that the two diseases are now inextricably linked. Among patients attending a chest clinic at the Sassoon General Hospital in Pune in the year 2000, 33% of the men and 20% of the women were infected with HIV, according to Srikant Tripathy of NARI.

Infection with HIV also greatly increases the lifetime risk of developing active TB—by about six-fold (60% versus 10%) in the patient population at the Tuberculosis Research Centre in Chennai, reported Soumya Swaminathan, the center's deputy director. Studies are underway there to evaluate prophylaxis for reducing active TB in HIV positive populations. Speakers at this session emphasized that current TB control strategies may not be enough to avoid the worsening of an already bad situation. One encouraging note is the trend toward integrating HIV and TB services, starting with the introduction of TB detection at India's HIV VCT centers.

Future Pathways: Improving Treatment

The growing threat of TB underscores the need to expand treatment services for the growing numbers of Indians with HIV/AIDS. Despite enormous financial and logistical obstacles, a few clinicians are researching strategies for providing ARVs in resource-poor settings. One of them is Subhash Hira of ARCON (a Mumbai-based HIV/AIDS collaboration between the Maharashtra state government and the University of Texas at Houston), an advisor to NACO on national AIDS policy, who stressed the link between offering care and greater use of testing and prevention services.

Current estimates are that only 9,000-10,000 HIV positive people receive antiretroviral therapy, despite substantial recent price reductions and India's production of generic HIV/AIDS drugs. While Hira said that budget constraints should not stop India from providing ARVs, which are cost effective in the long run, he called for targeting treatment initially to the sickest people who can still benefit. To assess just who they are, ARCON is following 125 HIV positive people who started ARVs in 1996–1997, looking for correlations between initial CD4 cell count and clinical benefit. Hira estimates that about one million people in India have CD4 cell counts below 350 cells/mm^3, a possible threshold for starting treatment.

For these and almost any other initiatives, community buy-in is key. Throughout the meeting, many speakers emphasized that investment in community education and mobilization is the only way to ensure implementation of the many interventions—PMTCT programs, testing and counseling services, vaccines, and care—needed to stem the rising tide of HIV/AIDS in India.

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