IAVI Report

THE NEWSLETTER ON INTERNATIONAL AIDS VACCINE RESEARCH VOL 6 / NUM 3 MAY/JUNE 2002

Barcelona 2002: Taking Stock of the Epidemic

BY PATRICIA KAHN AND EMILY BASS

In the high-stakes world of AIDS research, two years can bring distinct shifts in priorities and paradigms. And every 24 months, the Olympic-sized International AIDS Conference provides an opportunity to assess and reflect on these changes.

This year's Conference in Barcelona will undoubtedly take measure of the progress in AIDS since Durban 2000, the landmark gathering which focused the world's attention on the devastating epidemic in the global South. It will find a landscape changed in many ways—along with some discouragingly familiar constants.

Durban became a crucial turning point in mobilizing global commitment to fight HIV/AIDS in Africa, and in acknowledging the world's dismal failure to do so thus far. It also helped catalyze an emerging consensus that real progress will demand not only a massive scale-up of efforts and funds, but a more broad-based approach that recognizes the inexorable link between prevention and treatment, and that brings new sectors—from government finance ministries to international development agencies and business—into a battle that had been left mostly to public health agencies and affected communities.

This was also the view from the 2001 United Nations General Assembly Special Session on HIV/AIDS (UNGASS). The first UN session of its kind devoted to a public health issue, UNGASS concluded with a strongly-worded declaration promising intensified efforts in AIDS prevention, care, support and human rights protection for infected people and affected communities. At the same time, UN Secretary General Kofi Annan called for the creation of the Global Fund to Fight AIDS, TB and Malaria, an initiative which has so

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IAVI ESTABLISHES HIV NEUTRALIZING ANTIBODY CONSORTIUM

BY EMILY BASS

IAVI, the National Institutes of Health Vaccine Research Center (VRC) and a number of leading laboratories have formed an HIV Neutralizing Antibody Consortium (NAC) that will intensify work on one of the AIDS vaccine field's most enduring challenges: making antibodies that neutralize a broad range of HIV strains. The consortium will target funding to projects that make more direct links between basic science research on neutralizing antibodies (Nabs) and vaccine product development, and will facilitate closer collaboration among some of the field's foremost antibody researchers and their institutions, including: Dennis Burton (Consortium Director, Scripps Research Institute), Ian Wilson (Scripps Research Institute), Robert Doms (University of Pennsylvania), John Moore (Cornell University Medical College) and Joe Sodroski (Harvard Medical School), as well as Gary Nabel, Richard Wright and Peter Kwong of the VRC.

Neutralizing antibodies are Y-shaped immune proteins that bind free HIV and prevent it from infecting cells. They are thought to be an important component of the protection generated by many licensed viral vaccines, including polio and hepatitis B. In the AIDS field, experiments with macaques have found that passive transfer of HIV-specific antibodies can protect against challenge with SIV/HIV hybrid viruses. Since NAbs attack virus before it has entered cells, they could conceivably stop HIV—which must enter

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far brought US$2 billion in new resources to spend on the major diseases of poverty.

But in spite of these steps, there are sobering distances still to be covered. AIDS continues to spread relentlessly, not only in its established strongholds of sub-Saharan Africa and the Caribbean nations but in new regions and populations. For example, the world's fastest growing HIV epidemic in 2001 was in Russia and other regions of Central Asia, while the burgeoning number of newly-infected people in South Asia—home to about half the world's population—could outnumber that in sub-Saharan Africa within the decade if unchecked. On a political level, the world has not yet committed the resources needed to achieve the ambitious goals declared at Durban and UNGASS. Antiretroviral treatment and even rudimentary care remain out of reach to most of the world's people living with HIV/AIDS, and new prevention strategies have yet to emerge.

"Success in making an AIDS vaccine will require vision, scientific breakthroughs and far more resources."

Another key issue voiced at Durban is the need to balance present and future priorities. In practice this means reducing HIV spread through existing means and caring for those already infected, while at the same time mobilizing funds and political will for the vaccines and microbicides that will save future generations.

For AIDS vaccines, the past two years have brought growing support and scientific activity—although a successful vaccine is probably at least five years away (if the ongoing VaxGen trial does not show efficacy of the AIDSVAX® vaccine). And there are no guarantees of success. Some highlights since Durban:

- Several vaccines have moved (or soon will) into Phase I clinical trials, while Merck's DNA/adenovirus-based approach and Oxford/Nairobi/IAVI's DNA- and MVA-based vaccines are entering expanded Phase I/II studies.
- In addition to Merck, GlaxoSmithKline has an HIV vaccine in Phase I testing, while Wyeth-Lederle, Chiron, Aventis Pasteur and several small biotech companies are developing their own candidates.
- VaxGen's ongoing Phase III trials in Thailand, North America and Europe have passed the halfway point and should yield first results early next year. Whatever results the vaccine itself shows, these trials have demonstrated the feasibility of running large, ethical AIDS vaccine studies in high-risk populations.
- Developing country involvement is growing. Kenya, Trinidad and Tobago, Haiti and Brazil are now conducting Phase I or II trials, and several other countries—including South Africa, India, China, Côte d'Ivoire and several Latin American nations—have launched vaccine programs. Uganda, which ran Africa's first AIDS vaccine trial in 1999-2000, has several trials in the cards.
- A second AIDS vaccine approach (Aventis Pasteur's canarypox plus VaxGen's gp120) will soon enter Phase III testing in Thailand.

But many of the biggest challenges in developing an AIDS vaccine still lie ahead. There are many scientific unknowns. There is a great need to get safe, promising products into efficacy trials as soon as possible, and to build capacity for conducting these trials in countries highly affected by HIV/AIDS. And it is urgent to lay the policy foundations for making an effective vaccine widely available as soon as one is licensed.

As with the AIDS field overall, Durban also marked a broadening of the vaccine effort, with more governments, businesses and other new players from different parts of the world becoming engaged alongside the scientists, health workers and communities who are developing and testing vaccine candidates.

This issue of the *IAVI Report* highlights a few examples. We begin with a look at the field of female microbicides, which is now moving several products into later-stage testing (and has completed one Phase III study) in several African countries. In getting this far, it has already amassed valuable experience in running clinical trials that involve women at high risk for HIV—experience that also offers important lessons for vaccines.

In another example, we report on a community-led initiative to start an AIDS vaccine trial site in southern Brazil. It's something of a "tail-wags-dog" scenario, since trial sites nearly always begin with researchers, institutions and/or funders providing the first impetus and only then approaching the community. From India, a country with an estimated 3.9 million HIV-infected people, comes news of a recent gathering that brought together Parliamentarians and policymakers—along with both the Prime Minister and opposition party leader, an almost unprecedented double-bill—to take a closer look at AIDS vaccine development and the experiences of other developing countries already planning or conducting trials.

On the scientific front, we look at two difficult areas. Guest contributor Chris Beyrer, an AIDS epidemiologist and Southeast Asia expert, writes about HIV spread among injecting drug users (IDU), a key factor in most epidemics outside Africa. He argues that vaccines must be tested in both IDU and sexually-transmitting populations if we are to ensure that these products will work against both routes of infection. And he presents examples of willing, engaged IDU cohorts—starting with the Bangkok VaxGen trial population—and of potential new IDU trial sites that suggest these studies should be feasible. There's also a short report on a new IAVI-backed initiative to boost research into one of the toughest, most elusive tasks facing AIDS vaccines: how to induce antibodies that neutralize a broad range of HIV isolates.

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Learning from Microbicides: A Young Field's Experience Working with High-Risk Women

BY EMILY BASS

AIDS vaccines and microbicides share many key goals. Both seek to develop prevention strategies that will stem the tide of new HIV infections around the world, and both share a keen awareness of women's vulnerability to HIV. But despite these similarities, the two fields have evolved separate strategies for mobilizing funds, political will and scientific support for their goals.

Today, however, microbicides and vaccines are starting to converge on common ground. Both are pursuing trials in the developing world, and as they do so, microbicides—long considered a "little sister" to vaccines—are taking on a new role as a font of insights regarding the challenges facing both fields.

This has been catalyzed by exciting developments in the microbicide arena, with 2002 having several highlights. The New York-based Population Council completed a Phase II trial of a seaweed-based microbicide called Carraguard in high-risk women in South Africa and Thailand, and is now preparing for a 6,600-woman Phase III study scheduled to start in early 2003 (see table on p. 4 for details) The UK's Department for International Development unveiled a five-year, US$23.5 million microbicides project that will draw collaborators from South Africa, Tanzania, Uganda, Cameroon and Zambia. Another big step was the formation of the US-based International Partnership for Microbicides (IPM), a new public-private partnership with pledges of nearly $30 million from governments and private sector funders over the next five years. The IPM plans to use these funds to speed research and spearhead planning on the manufacturing, regulatory and access fronts.

This activity has been a long time in coming. Microbicides are a novel concept that was slow to receive widespread support from politicians or AIDS researchers, some of whom have falsely categorized them as "kitchen-sink" contraceptive research. Save for a few small biotech companies, the private sector has stayed away from developing microbicides.

In spite of these hurdles, a dedicated group of advocates and researchers has made steady progress. Earlier this year, many of these players collaborated on a series of expert papers, produced with funding from the Rockefeller Foundation's Microbicides Initiative, that explored a range of issues around economics, acceptability and access. The papers also included modeling studies which demonstrate the strong impact even a partially effective microbicide could have on reducing the numbers of new infections and saving health-care expenditures, even excluding antiretrovirals. These papers helped identify priorities for the newly-formed IPM.

This flurry of activity, and the new impact analyses, have captured the attention of even the most seasoned players in the field. "For the first time—and I get goosebumps as I say this—we have the hard data to make a strong case for investments in microbicides," said Geeta Rao Gupta, President of the International Council for Research on Women, at a Microbicides Initiative event this past February.

Good news for microbicides is good news for AIDS vaccines, too. Microbicides are moving forward with trials in some of the same populations AIDS vaccine developers will also need to engage, which include commercial sex workers (CSW), adolescent girls and other women at high risk, especially in developing countries. Roughly 4,000 high-risk women have already participated in microbicide studies—significantly more than for AIDS vaccines, where the two Phase III trials to date have involved cohorts that are roughly 95% male.

Finding points of comparison

Overall, the microbicide field has conducted 14 studies of vaginal microbicides in humans, including several large trials in women at high risk. There are 50-60 different compounds in various stages of development, and they can be grouped into about five categories based on their mode of action. Products also vary in their scope—some aim to protect not only against HIV but also other STDs, while some are potential contraceptives.

In recent years, funding shortages have kept many of these candidates idling in pre-clinical development instead of entering human trials. But those which have moved forward are progressing towards Phase III studies more rapidly than AIDS vaccines are. One reason: Early microbicides studies can determine product safety, but they yield no data (such as immunogenicity) that hint at efficacy. Without a way to evaluate products in Phase I or II trials except for safety, microbicide investigators tend move more quickly to Phase III trials. (Carraguard, which enters Phase III trials this year, had equal numbers of infections in the gel and placebo arms of its Phase II trials.)

Because of this rapid pace, the microbicides field—although relatively young—has already conducted several large trials in the developing world. These differ from vaccine studies in the type of commitment needed from volunteers, since participation entails regular gel use over months or years, providing detailed information about sexual

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practices, and use of a product that may be noticed by male partners, opening the door for conflicts over trial participation. Yet these demands also mean that planners must find highly effective ways to engage women in trials.

Many of the lessons from these trials apply to vaccines—lessons that were center stage at Microbicides 2002 (12-15 May, Antwerp, Belgium), the field's major biannual meeting. There, several hundred participants gathered to discuss the victories and setbacks of the previous two years, including an in-depth look at two of the field's most significant trials to date: COL-1492, a Phase III study of Nonoxynol-9 (N-9) completed in 2000; and this year's Phase II Carraguard study.

Selected Phase II and III Microbicide Trials

Product (Description)	Study	Sites	Population*
	COMPLETED TRIALS		
Nonoxynol-9 (N-9) spermicide film	Family Health International (USA) Effect of N-9 film on male-to-female transmission of sexually transmitted diseases[1]	Cameroon	1,292 commercial sex workers
N-9 spermicide gel	Effect of N-9 gel on male-to-female transmission of STDs[2]	Cameroon	1,251 high-risk women recruited from community clinics and pharmacies
N-9 spermicide gel	Institute of Tropical Medicine (Belgium) COL-1492/Phase III[3]	Thailand, South Africa, Côte d'Ivoire and Benin	900 commercial sex workers
Carraguard (vaginal coating/ absorption inhibitor)	Population Council Phase II[4]	South Africa	400 sexually-active women
		Thailand (CDC site)	165 sexually-active women recruited from family planning clinics
	PLANNED TRIALS		
BufferGel (enhancer of vaginal defenses) and PRO 2000 (vaginal coating/ absorption inhibitor)	HPTN 035 Phase II/III safety and efficacy study planned start July 2002	India, Malawi, South Africa, Tanzania, Zimbabwe	11,000+ sexually-active women recruited from postnatal, STD and family planning clinics
Carraguard (vaginal coating/ absorption inhibitor)	Population Council / Phase III planned start early 2002	South Africa, Botswana (CDC sites), other sites	6,600 sexually-active women from family planning clinics, general health clinics and other recruitment sites
Dextrin sulfate (Vaginal coating/ absorption inhibitor)	Medical Research Council / M-L Labs Phase II	N/A	N/A

**All studies done on HIV-negative women.*
1 *N. Engl. J. Med. 339:504;1998*
2 *JAMA 287:1117;2002*
3 *AIDS 14:85;2000*
4 *Presented at Microbicides 2002 conference, Antwerp, Belgium (12-14 May 2002)*
Additional trial information provided by Alliance for Microbicide Development (www.microbicide.org)

Recruitment and retention

Leopold Zekeng (Laboratoire de Santé Hygiène Mobile, Cameroon) reported on two successive N-9 trials in Cameroon, each of which enrolled approximately 1,200 women. The first, which tested a film formulation, enrolled commercial sex workers; the second tested an N-9 gel, in high-risk women not engaged in commercial sex work.

Both cohorts were followed for two years, with a 20% loss to follow-up in CSWs and a 5% loss in non-CSWs. The study employed an all-female enrollment and outreach staff, who obtained volunteers' permission to make home visits if they failed to appear for scheduled appointments. Zekeng said that having a female team was important, since it avoided suspicions that might be aroused by women receiving unfamiliar male visitors. A physician was also available for house calls to participants.

This year's Carraguard trial also reports encouraging results. The CDC-sponsored site in Chiang-Rai, Thailand retained over 90% of participants. The South African sites also reported high retention (complete data analysis is still underway). Nicol Coetzee (University of Cape Town), a principal investigator at the Guguletu, South Africa site, emphasized the importance of staff committed to intensive follow-up for no-shows, which can involve multiple phone calls or prolonged searches for participants in squatter camps. Looking ahead to the upcoming Phase III study, which will enroll 6,600 women at multiple sites in southern Africa, including 2,000 in Guguletu, Coetzee acknowledged that it will be a challenge to meet the increased level of investment needed for effective recruitment and follow-up.

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India's Political Leadership Gathers for Update on HIV/AIDS and Vaccines

A report on the International Policymakers Conference

BY SUBHADRA MENON

Here in the world's most populous democracy, rival political parties seldom show unity, whatever the cause. But a rare display of shared commitment recently took place at the International Policymakers Conference on HIV/AIDS (New Delhi, 11-12 May 2002),* where India's Prime Minister Atal Bihari Vajpayee and Opposition leader Sonia Gandhi each spoke about the epidemic and the extreme urgency of uniting the country in battling the disease and its devastating consequences. It is estimated that nearly 4 million people in India are living with HIV/AIDS.

The conference was attended by about 200 delegates, mostly policymakers from India (including several state Ministers and about 30 Parliamentarians), but also including representatives from seven other developing countries (Thailand, South Africa, Nigeria, Kenya, Uganda, Brazil and Nepal) that are either conducting or preparing for vaccine trials (except Nepal). The meeting served to inform delegates about the state of the epidemic, both globally and within India, and of efforts on prevention, care and coping with the devastating consequences of HIV/AIDS for affected families, communities and entire countries. It also highlighted AIDS vaccine development and provided an opportunity for political leaders from participating countries to swap experience and expertise on vaccine programs and clinical trials.

Prime Minister Vajpayee emphasized the unlikely political alliance. "For all of us in India, controlling the spread of HIV/AIDS and taking good care of its victims has become an urgent national task," he said. "It is a concern that is shared equally by the Central and State governments, as also by all political parties." Opposition leader Gandhi also underscored the significance of the meeting's mixture across party lines. "This presence should reaffirm our national resolve to combat, in the most vigorous manner possible, the serious HIV/AIDS crisis in the country," she said.

But while there was strong consensus on many issues, including the urgency of scaling up current prevention efforts and building a strong AIDS vaccine program, there were clear differences on issues of treatment and care, especially on the feasibility of making anti-retroviral drugs (ARVs) more widely available. The government's national program does not include plans for expanding access to ARVs, except in the case of mother-to-child transmission (where a strong national drive to provide treatment is underway). In his speech, Prime Minister Vajpayee emphasized cost as a key obstacle. "Even after removing all excise duties on them—our Government has done so in the recent budget—such multi-drug therapy will still cost between 1,200 and 20,000 rupees (US$30 to $400) a month," he said.

In contrast, Gandhi highlighted the availability of cheaper generic alternatives, especially those made by Cipla, a Mumbai-based pharmaceutical company that is now a world leader in producing them. "It is ironic that Indian pharmaceutical companies have emerged as suppliers of AIDS control drugs to the world and are being welcomed in other countries, while we ourselves are reluctant to involve them in the national AIDS control program," she said. "This is a paradox that needs to be resolved."

Vaccine Programs in Developing Countries

Within India, AIDS vaccines were declared a high priority several years ago, and the government has committed to help develop and test suitable candidates (including through collaboration with IAVI; see *IAVI Report*, Feb/Mar 2001, p.1). But with a wider conversation about these trials now beginning in India, questions ranging from scientific and logistical issues to trial ethics and political acceptability are on the minds of many stakeholders. Against this backdrop, several talks on how other developing nations got started in AIDS vaccine work and what lessons they have learned so far attracted strong interest.

One common thread running through these presentations, despite the countries' very different levels of readiness, was a clear recognition that broad political commitment must be in place to support vaccine trials and mobilize public opinion behind them. Another was the importance of placing vaccine programs within a broader context of AIDS-related initiatives on prevention and care.

Two speakers discussed the situation in Thailand. Parliament member Cholnan Srikaew described the country's "100% condom campaign" launched in the early 1990s and its wide outreach of STD diagnostic and treatment centers. Both of these arose, he said, through "a committed alliance between the government and the public to fight AIDS."

Thailand's Senator Jon Ungphakorn presented a mixed picture of the situation today. With new infection rates in most groups markedly below those of a decade ago, "our country is getting into

> *"Broad political commitment must be in place to support vaccine trials and mobilize public opinion behind them."*

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**Co-sponsored by India's National AIDS Control Organization (NACO), the Indian Council on Medical Research (ICMR) and IAVI.*

INJECTING DRUG USERS AND HIV VACCINE TRIALS: WHAT DOES THE SCIENCE SAY?

BY CHRIS BEYRER

The great burden of HIV/AIDS in Africa has led the international community to scale up the search for effective prevention strategies for this hardest-hit region. Appropriately, this has included a focus on developing new tools—especially vaccines and microbicides—that will reduce heterosexual transmission, which accounts for the vast majority of new infections on the continent. Many groups are now working to expand capacity for testing candidate HIV vaccines in Africa and to involve at-risk men and women in these clinical studies.

But in many parts of the world outside Africa, the epidemiological picture of HIV in 2002 is strikingly different. In Russia, Ukraine, Belarus and the Central Asian Republics of Kazakhstan and Tajikistan, and further east in China, Iran, Malaysia, Indonesia and Vietnam, the *majority* of reported HIV infections and AIDS cases in 2001 arose not from sexual transmission but through needle-sharing behaviors among injecting drug users (IDU). While the numbers of IDU infections in any one country may not be large on a population basis, these states have enormous young populations, many with rapidly rising substance abuse rates. A good example is Vietnam, a country of over 78 million people, where IDU accounted for 88% of all reported HIV infections in 2000 and where heroin trafficking from the Golden Triangle has led to a dramatic increase in use among young Vietnamese (*JAIDS* 25:360;2000).

In other places where IDU do not represent the majority of infections, they have nonetheless played important roles in HIV spread. This is true in settings as diverse as Burma and Baltimore, the remote Indian Northeast, and cities and towns in Spain, Italy, the Netherlands and Brazil. IDU-related outbreaks were also key to the initial introduction of HIV into all Asian countries except Cambodia. And they are often crucial to the dissemination of new HIV-1 subtypes and recombinants—for example, the recent explosive spread of subtype A virus in Russia and Ukraine, and a B/C recombinant now epidemic among IDU in southern and western China. Overall, the number of countries reporting HIV infections among IDU to the World Health Organization rose from 52 in 1992 to 114 in the year 2000, underscoring the widening global nature of IDU risk.

Thus the epidemiology of HIV in 2002 tells us that for a vaccine to be truly effective in curbing the global epidemic, it must work against both sexual and IDU transmission. Yet these two routes of infection may require some distinct approaches. Scientifically, we don't know whether the same set of immune responses will work against both routes. The two certainly do not offer the immune system identical opportunities, since blood-borne transmission bypasses the immune defenses present in the genital tract's mucosal lining, where the first exposure to sexually transmitted HIV takes place—defenses which may be important contributors to vaccine protection. And from the perspective of clinical trials, IDU populations clearly present their own set of challenges.

Here I argue a few key points from among many issues raised by IDU and AIDS vaccines, and briefly review data bearing on them.

(1) We cannot assume that vaccines which prevent or reduce sexual transmission will necessarily work as well against IDU spread. The evidence so far is simply too scant to draw any conclusions one way or the other, and some of the available data suggest potentially important differences—making it imperative to test vaccine candidates against both types of transmission. A vaccine that reduces only sexual transmission would arguably have limited public health impact in 114 countries, especially across Eurasia, and might lead to a scenario in which heterosexual transmission is controlled but outbreaks of HIV continue wherever there is IDU spread.

(2) There is a widespread perception that IDU make for poor participants in HIV vaccine trials, for several reasons—a view that is contradicted by the data.

(3) Trial sites could potentially be built onto a number of ongoing projects around the world that are now working with IDU populations. One—the Bangkok sites of VaxGen's ongoing Phase III vaccine trial involving 2,500 IDU—is already well-established, while others could, with appropriate expansion, become AIDS vaccine trial sites in the future.

COMPARING SEXUAL AND BLOOD-BORNE TRANSMISSION

Vaccine responses and acute infection

Animal models using monkeys challenged with SIV (simian immunodeficiency virus) or related viruses point to some differences between intravenous and mucosal exposure. An important caveat, though, is that it remains unproven how well these models predict what happens with IDU versus sexual transmission in humans.

Nevertheless, studies of experimental vaccines in monkeys suggest that it is often easier to protect against mucosal exposure to SIV than against intravenous (i.v.) challenge. For example, Benson, Franchini and colleagues compared protection induced by

an SIV vaccine made in the NYVAC viral vector (*J. Virol.* 72:1470;1998). Looking at 12 vaccinated monkeys challenged i.v. with SIV (strain mac251), they found that all of them became infected. Over time, 4 showed some vaccine protection—they gradually brought SIV replication under control and slowed progression to AIDS—while 8 went on to AIDS. But in 12 vaccinated animals challenged intra-rectally, five seemed to clear the SIV infection completely after showing transient viremia; the other 7 animals progressed to AIDS, although more slowly than those in the i.v. group.

This vaccine—like most of the candidates being developed for humans—most likely confers its partial protection by stimulating the cellular immune responses. For the other arm of the immune system, John Mascola's group compared how well HIV antibodies can protect animals against i.v. versus mucosal infection. (*Vaccine* 20:1922;2000). Since there are no vaccine candidates so far that induce broadly neutralizing antibodies, the type thought to offer the most promise, Mascola instead infused 26 monkeys with monoclonal antibodies derived from HIV-infected people. He then infected the animals either i.v. or vaginally with a strain of SHIV (an SIV/HIV hybrid). Again, the results showed somewhat better protection against the vaginal challenge than against i.v.exposure.

What could account for these differences? The answer is unknown, but the immune responses in the genital mucosa are one candidate. Another factor (perhaps related) is time: how fast infection is established after exposure by each of these routes, and how long this gives the immune system to mobilize.

Indeed, evidence that sexual infection takes longer to become established (as measured by the time from infection until peak viral load) comes from a study of i.v.- and vaginally-infected macaques challenged with a pathogenic SHIV (*J. Virol.* 70:3045;1996). Peak load occurred at 7 days for animals exposed through injection—but not until 14 days for monkeys challenged vaginally. Similarly, the severe CD4 T-cell declines seen with this (and other) SHIV strains occurred after 14 days for animals challenged i.v., but not until at least 21 days in the vaginally exposed group. If earlier peak viral loads also occur in IDU, then an effective vaccine for IDU might have to mobilize the immune system faster than for protection against sexual transmission.

However, moving from timing to clinical measures, the differences disappeared: Both i.v.- and mucosally-challenged animals in the above study reached about the same peak viral loads and showed similar clinical findings (such as CD4 decline) as their infections progressed. In humans, there is too little data on viral load shortly after infection (days or weeks) to see an effect of transmission route, although by a few months there appear to be no differences.

This raises an alternative view that, at least for the current generation of vaccines aimed at controlling HIV (rather than completely preventing infection), viral load is what really matters—and if peak load in the blood doesn't differ between i.v. and sexual transmission, then vaccines may work similarly against both. In other words, "viremia is viremia," as this idea is phrased by Larry Corey (head of the HIV Vaccine Trials Network based in the US), no matter how it originates.

Transmission efficiency

IDU transmission is often perceived as being more efficient than mucosal transmission, but careful analysis of the data suggest that this is not the case.

One source of confusion is that HIV infection through blood and blood products is sometimes grouped with IDU transmission. However, this should be considered separately, since it often involves whole units of infected blood or plasma, while IDU transmission mostly occurs through tiny residual volumes of blood in used injection equipment.

Another reason for the misperception is the rapid spread of HIV among injectors once HIV has been introduced into an IDU population, and the very high rates of infection among IDU worldwide. But the speed of spread is affected by two distinct factors: transmission efficiency per act, and frequency of the risk behavior.

Transmission efficiency per act has been estimated in various ways, most of which rely on modeling techniques. These are summarized in the table on p. 8 (adapted from *AIDS Res. Hum. Retrovirus* 14 [suppl. 3]:S223;1998). Kaplan and Heimer developed a model for IDU transmission in 1992 which estimated a per-act transmission probability of .0067 per injection. This is somewhat higher than the rate per heterosexual sex, .001/act, but roughly similar to transmission from Thai female sex workers to male clients (.03 -.06) and significantly lower than estimates among heterosexual Kenyan men who also had a genital ulcer (.10/sex act).

These studies must be interpreted with caution, but taken together they suggest that IDU transmission per act is, like sexual transmission, relatively inefficient. The much higher reported rates of hepatitis C (generally over 90%) compared with HIV among IDU cohorts in the US, Thailand, and Amsterdam also lend indirect support to these modeling studies.

But while the probability of transmission may be similar for individual acts, most studies find that heroin addicts inject about 1-3 times per day, and cocaine addicts even more frequently. Few people at sexual risk, sex workers aside, have anywhere near these levels of exposure.

Later clinical course of HIV and AIDS

Several large prospective cohorts have been analyzed for differences in the clinical course of HIV/AIDS by transmission route. Comparing MSM and IDU in the US, there appeared to be

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◀ **IDUs AND HIV VACCINES** *continued from 7*

somewhat slower progression to AIDS among IDU, although clinical outcomes did not differ strikingly. Whether this will be relevant to vaccines that work by reducing viremia and thereby changing the clinical course to AIDS remains to be tested, along with other unrelated factors that could play a role (such as gender, nutritional and immunological status and possibly HIV-1 subtype differences).

Vaccines against blood-borne diseases: the EIAV example

As an interesting side point, it is worth noting an example of a highly effective vaccine against a blood-borne disease of the immune system. This is the Equine Infectious Anemia Virus (EIAV), an animal retrovirus (in the same visna virus family as HIV and SIV) for which spread by unsterile injection equipment has been documented in veterinary settings. EIAV causes epidemic anemia in horses and ponies, and in nature is spread between horses by the bite of horse flies. Interestingly, the fly is not a host of the virus—the virus has no life cycle stage in the fly—but rather is a mechanical transmission vector whose mouthparts act like a hypodermic needle to spread the virus from horse to horse (*J. Med. Entomol.* 24:613;1987).

It is therefore encouraging that Chinese government scientists developed an EIAV vaccine more than 20 years ago (using Pasteur's method of serial passage in culture to attenuate the virus), and that this vaccine has succeeded in virtually eradicating the disease from China's horse herds (personal communication from Yiming Shao, China).

IDU AS PARTICIPANTS IN HIV VACCINE EFFICACY TRIALS

Do IDU make for poor participants in HIV vaccine trials? Concerns have been raised over low retention rates, high rates of medical exclusion (largely due to hepatitis C infection) and, in the US, low HIV incidence rates.

However, a review of data from the field suggests that IDU are already active and engaged trial participants. The clearest example is Thailand's ongoing trial of the AIDSVAX® gp120-based vaccine, which involves 2,500 seronegative IDU in Bangkok's methadone clinics. Retention in this cohort has been strikingly high, with a reported 1.5% loss to follow-up per year (*AIDS* 15:397;2001). If maintained, this will give an overall retention of well over 90% during the three-year trial, remarkable for any HIV at-risk population. At the same time, despite intensive counseling and harm-reduction measures, there is high and sustained seroincidence among these IDUs, fueled largely by imprisonment of participants on drug-related charges (*J. Acquir. Immun. Defic. Syndr.* 30:240;2002).

But important barriers to IDU participation in research do exist. Injection drug use is a highly criminalized and stigmatized behavior globally. IDUs generally face many of the same behavioral and psychological challenges common to substance abusers, but also legal and social harms due to the illegality of the substances they use. Moreover, while several strategies have shown effectiveness in preventing HIV infections in IDU—including harm reduction, needle and syringe exchange programs and substitution therapy such as methadone maintenance therapy (MMT)—use of these tools is forbidden or severely restricted by law in most countries around the world (*Lancet* 349:1797;1997; *Drug Alcohol Depend* 59:17;2000). Across Asia, for example, only Hong Kong has both MMT and harm reduction programs for IDU.

Conversely, where harm reduction and MMT are available, as they were to many US IDU in the HIVNET vaccine preparedness studies, seroincidence can be low (*Am. J. Epidemiol.* 153:619;2001). In these studies, MSM seroincidence from 1995-1997 was measured at 1.55/100 person-years (PY), while among male IDU, the rate was 0.38/100PY, which many researchers consider too low for efficacy trials. Rates were higher among women IDU, at 1.24/100PY, but this group had the lowest enrollment of all groups in the trial. Retention rates among male IDU were encouraging, at 12.3% loss to follow up over 18 months, similar to MSM. Most of the women IDU participants met the enrollment criteria for both injection and sexual risk, suggesting that their dual risks

Per-Act Probabilities of Transmission

Study Population	Route of Transmission	Per-Act Transmission Transmission Probability
Heterosexual couples		
United States (Peterman et al. 1998. Wiley et al. 1989.)	Penile→Vaginal	0.001
United States (Wiley et al. 1989. Padian et al. 1987.)	Penile→Vaginal	0.0008 - 0.001
United States (Fischl et al. 1987.)	Penile→Vaginal and Vaginal→Penile	0.001
Europe (Downs et al. 1996)	Penile→Vaginal and Vaginal→Penile	0.0005 - 0.001
Heterosexual Men		
Kenya (Cameron et al. 1989)	Vaginal→Penile, from FSWs to men who also acquired a symptomatic STD	0.1
Thailand	Vaginal→Penile, from FSWs to men	0.03-0.06
Homosexual Men		
United States (DeGruttola et al. 1989)	Penile→Anal, receptive	0.005 - 0.03
Injection Drug Users		
United States (Kaplan and Heimer. 1992)	Shared Injection Equipment	0.0067

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Community Advocates Spur Effort to Establish New Vaccine Trial Site in Brazil

BY ALEXANDRE DO VALLE MENEZES AND RONALDO MUSSAUER DE LIMA

From 2-4 May 2002, a group of AIDS community advocates, government policymakers and others involved with HIV/AIDS met in the southern Brazilian town of Santa Cruz do Sul to begin forging plans for launch a vaccine trial site in their region. It was an unusual role reversal: in the normal course of events, such endeavors generally begin with researchers or funders, with communities coming on board later in the process after plans are underway.

The meeting was convened by a well-established AIDS NGO called GAPA/RS (Portuguese acronyms for Support Group for AIDS Prevention in the state of Rio Grande do Sul), an organization that sits on the National AIDS Vaccine Committee of the Ministry of Health (MoH), Brazil's main advisory body to its AIDS vaccine program.

Although the meeting was the first public step in mobilizing local support, the notion of a trial site in Brazil's south is not new: initial plans for the country's vaccine program, launched in the early 1990s, foresaw a site in the region, building on its strong health care and research infrastructure. But, while sites were established in Rio de Janeiro and, more recently, Sao Paulo (both now part of the NIH-sponsored HIV Vaccine Trials Network), plans for the South were never developed.

Their revival was sparked when Brazil's MoH announced late last year that it planned to boost AIDS vaccine research initiatives around the country. By that time, arguments for a site in the South were even stronger. One was its growing AIDS problem: while the epidemic appears to be subsiding in many parts of Brazil, the three southern states showed a 13% rise in the number of new AIDS cases last year (based on the number of people registering to get treatment in local health clinics). This increase is fueled partly by a substantial IDU epidemic in the region, which is not the case elsewhere in the country. In another new twist, a high proportion of HIV infections in the IDU group come from HIV subtype C rather than subtype B, which accounts for the vast majority of infections in the rest of Brazil.

During the 1990s, the infrastructure to support a southern trial site also grew stronger. Besides the existing universities and research hospitals, there was a build-up of the public health system, including the central state laboratory responsible for all HIV lab analyses as well as comprehensive clinical care for people with AIDS. Another plus is that the South has Brazil's best harm reduction program, a response to the growing epidemic in a region with the country's highest social development and income rates. The MoH (through its National AIDS Program, NAP) has supported state-of-the-art interventions, including needle exchange programs and projects that help HIV-positive IDUs adhere to the antiretroviral regimens offered free of charge by the public health system.

Against this backdrop, the MoH announcement of an expanded AIDS vaccine program led the NAP once again to view the South as a potentially important region, spurring GAPA/RS to begin organizing around the idea. That, in turn, led to the May meeting, which was attended by nearly 80 representatives from local PWA groups, sex workers associations, research organizations, the state health council, the central HIV laboratory and local and national health authorities.

The meeting's goals were two-fold: to have participating organizations consider and incorporate vaccine issues in their daily agendas, and to take the first steps towards creating a future vaccine site and regional Community Advisory Board (CAB). Following NAP's suggestion, it was agreed that the best strategy is to begin with studies on HIV seroincidence and other parameters that influence the feasibility of a region and its populations for vaccine trials—studies the NAP has agreed to fund. If these go well, build-up to a full vaccine trial site could then take place, most likely in collaboration with an international partner.

To advance this agenda, part of the meeting was devoted to setting specific advocacy goals for increased involvement of local public health agencies and research institutions. Each participating community organization left the meeting with an advocacy plan and a mandate to forge links with the local councils of research ethics, which could help support the establishment of regional CAB's. They also made plans for monitoring and reviewing their progress and for keeping up political pressure and community momentum.

The advocates recognized that there could be difficulties along the way. Chief among them is the notion of organizing a trial site without a long-term partner or a vaccine to be moved into the clinic. But the government is in early stages of conversation with several companies about conducting vaccine trials, and participants left the meeting committed to continuous vaccine advocacy and to keeping the trial site issue moving—reasons for optimism that the South may join the global vaccine effort sometime soon. ◆

With reporting by Liandro Lindner of GAPA/RS, who coordinated the meeting.

Alexandre do Valle Menezes has been an AIDS advocate with Brazil's Grupo Pela Vidda Rio de Janeiro since 1993. He is currently a graduate student at NYU's Tisch School of the Arts and consults for IAVI on policy issues.

Ronaldo Mussauer de Lima is Director of Information Technology (IT) at IAVI and a long-time AIDS advocate. He was formerly president of the Brazilian AIDS community-based Grupo Pela Vidda (Rio de Janeiro) and head of the Brazilian National AIDS Program's IT department.

> *"At the meeting, AIDS advocates set specific goals for increasing involvement of local institutions in vaccine-related research."*

New Models for Vaccine Delivery

AN INTERVIEW WITH

Tore Godal

When the Global Alliance for Vaccines and Immunizations (GAVI) was founded in 2000, it pioneered a new model for accelerating the delivery of public health commodities to developing countries. Specifically, the Alliance seeks to increase coverage of basic childhood immunizations in low-resource settings that have long lagged behind in being able to provide these vaccines, which include combinations like measles-mumps-rubella and diptheria-tetanus-pertussis (DTP), and hepatitis B. Working with the Vaccine Fund, a sister organization which mobilizes the funds to buy and deliver vaccines rapidly, GAVI supports programs in 60 of the world's 74 poorest countries. Two years after its launch, it is the elder statesman in a global health arena now also populated by similar new models, such as the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM).

Tore Godal is GAVI's Executive Secretary. A Norwegian-born immunologist, he is former head of the UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases (TDR), and has also served as the initiating project manager for the Roll Back Malaria Project and as special advisor to Gro Harlem Brundtland, Director-General of the World Health Organization. In this discussion with* IAVI Report *Senior Writer Emily Bass, he describes what GAVI has learned about establishing effective vaccination programs in developing countries and how these lessons could apply more generally to programs that might follow in its footsteps, including the GFATM and future AIDS vaccine distribution schemes.

In 1999, GAVI laid out several concrete milestones. How have you fared in terms of meeting these goals?

We have the same milestones that were set in 1999—for example, that by the end of 2002, 80% of the poorest countries with adequate delivery systems will introduce hepatitis B vaccine, and by 2005, 80% will have at least 80% coverage with routine immunizations in all districts. [*Editor's note: Countries are deemed to have adequate infrastructure if they already provide at least 50% DTP coverage.*]

We are pretty much on target. So far, 40 out of 47 countries with adequate infrastructure are in the process of introducing hepatitis B vaccine—that's just over 80%.

That must be very gratifying.

It looks promising, I must say. But I'm sure that some countries will not perform as they have laid out in their proposal and 5-year plan, and then we will have to take action based on that.

We're now entering the implementation phase—a rather exciting part of the process, where we will assess performance and act on the results.

How will that be done?

We have selected one global indicator: DTP coverage. We assess this based on what we call a Data Quality Audit [*conducted by independent consortia that include the auditing firms Price Waterhouse and Deloitte and Touche*], a process of conducting visits at a country level to gather data from the primary place of immunization upwards through the system. We visit randomly selected sites, usually four districts in a country and six health facilities within each district. Then we compare these data with what the country is reporting in terms of their national immunization coverage.

Are there specific elements or approaches that make a GAVI-funded program likely to succeed?

We put our emphasis on countries' achieving specific milestones and then give them complete freedom as to how they accomplish this. They can use the money they get from us however they want.

What is interesting is that they have all decided to get money down to the district level as quickly as possible, because that is the only way to get increased coverage.

What are some examples of specific countries or diseases where GAVI-funded programs have been particularly successful?

One example is Tanzania, which was very systematic in its approach. They decided to take districts that were performing poorly, but where they thought something could be done about it. The GAVI money went for per diems to the health workers and for bicycles and petrol, so that health providers could do better outreach.

In Ghana, they decided to spend the money on computers for health facilities, so they could improve their record system and implement performance incentives for high-performing sites. And in Kenya, they decided to transfer the money directly from the Minister of Health to the district medical officer and to adopt a performance-based

payment system that bypassed the normal government channels, where money tends to get stuck between Nairobi and the districts.

Where has GAVI not had as much impact as it hoped for?

There are countries such as Laos, where preliminary data suggest that there may not be much progress. But we haven't yet done the Data Quality Audit for this year, so we don't have the hard data.

Overall, we're changing our focus. For the first two years, it was a matter of receiving proposals. Now we're setting policies for implementation. We will get information from countries on how they are doing, and we'll respond depending on whether they are successful or have problems reaching the targets they set for themselves.

This is a different phase for GAVI, with different requirements. For example, it requires tighter management to ensure that GAVI grants bring added value to the projects they fund, and less inclusiveness in terms of who is involved in policy discussions.

How does GAVI balance the need to move quickly against the time it takes to build buy-in and decision-making structures in-country?

When GAVI started, the general picture was that aid moved very slowly. We would hear about big numbers of available dollars, but we would never see them. I remember the Minister of Health from Mozambique at a meeting saying, "In 1988 we asked the World Bank for a loan to the health sector, but we did not get an answer until 1994."

In contrast, GAVI and the Vaccine Fund were launched in January 2000, and some countries received a first installment of financial support later that year. In April 2001 we introduced hepatitis B vaccine in the first country, Mozambique.

It's true that we impose some time constraints, but this is necessary to avoid having the process become too elaborate. Political leaders in the receiving countries were very keen to get the funds, so they pushed to get the technical assistance needed to develop their proposals quickly.

This year, a report on four GAVI-funded programs was published by Save The Children UK and the London School for Hygiene and Tropical Medicine. One concern it raised was that Ghana was pressured to accept a pentavalent vaccine [containing hepatitis B, Haemophilis influenzae type B (Hib) and DTP] which was not the product they requested in their grant.

This is a case of inaccurate reporting. Countries have criticized that study for rushing in, collecting data and not discussing them with authorities. Ghana's Minister of Health has explained that the country had been considering the introduction of hepatitis B and possibly Hib for years, and that this pentavalent vaccine was a deliberate choice on their part. He also said that Ghana is prepared to take over funding of the program after five years, when GAVI support comes to an end.

But we have seen some problems. Many countries say they want combination vaccines containing five shots in one, so they only need to give one injection. This makes delivery much simpler. When we started, we thought that obtaining these combination vaccines was only a question of financing—that if we had the funds, then we could deliver.

This has not turned out to be true. There is a limited production capacity for the different combination vaccines. So we had to make decisions about which types of vaccines were given to different countries, and these were not always the combinations the countries wanted. This created frustration. Countries thought they would get something they couldn't get.

The positive side is that industry has now responded by forming new kinds of consortia and increasing production capacity. But this takes time. We will not see the increased capacity before next year or, more likely, 2004-05.

What kinds of consortia? What specifically is happening?

I can give you one example. Chiron, a multinational company, produces Hib. Then there is Green Cross in Korea, which has patents and licenses for hepatitis B, and BioPharma in Indonesia, which makes DTP. They have formed a consortium to produce a pentavalent vaccine containing DTP plus Hep B plus Hib. Isn't that a marvelous collaboration?

It certainly is. Where will the vaccine be made?

I think at BioPharma, but it is not completely clear. It's possible that the vaccine will be produced in bulk in all three places, and one place will fill the vials.

This type of partnership could be relevant to AIDS vaccines, for example if a biotech company without production capacity developed a vaccine. This biotech could line up with a fairly sophisticated producer in the South that has a good manufacturing facility but no R&D capacity.

The London School report also raised the concern that GAVI is not providing enough support to health infrastructure.

It is fair to say that the infrastructure in many countries is more dilapidated than we had anticipated. For example, to deliver the more advanced new vaccines, there is a clear need for more sup-

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Vaccine-Preventable Child Deaths

1.7 million children die each year from vaccine-preventable diseases, including*:

- pneumococcal disease (1.2 million)
- measles (777,000)
- Haemophilus influenzae type b (Hib) (350,000)
- pertussis (296,000)
- polio (1,750: over 1/2 of all reported cases)

30-40 million children in the developing world are not covered by routine vaccination

* Data from the World Health Organization (WHO), the Global Alliance for Vaccines and Immunizations (GAVI) and the Measles Initiative

◀**GODAL INTERVIEW** *continued from 11*

port to secure the cold chain [*reliable storage facilities and transport mechanisms for vaccines needing refrigeration*]. Now partners are now coming in with this support as part of the alliance. GAVI cannot cover all infrastructure needs—ours is more of a catalytic role. So UNICEF is stepping up its support for cold chains, and bilaterals like the Japanese Institute for International Collaboration (JAICA) are also stepping up.

In general there is more focus on immunization-related activities, I think, thanks to the establishment of GAVI.

> *"The political commitment . . . is amazing. Vaccines are now seen like water and sanitation—they should be available to everybody."*

What is the best constellation of stakeholders to start addressing training needs?
In my mind, we haven't fully resolved the issues of capacity building and operational research needs for an activity like GAVI. When we start doing disease-burden studies relating to pneumococcal disease, to rotavirus disease, it will be an opportunity to build more long-term capacity. We're still pondering how to do this. One thing I would like to see is more partnering between academic institutions in the North and the South.

How does the Vaccine Fund buy its vaccines?
The Vaccine Fund [VF] is contracted with UNICEF for special procurements on behalf of GAVI and the VF. Because this involves purchasing large volumes of vaccines, we've halved the price of hepatitis B vaccine, for example.

One of the lessons we learned is that if you can make multi-year commitments to industry, you are likely to get better prices and services. We will now move into a multi-year commitment to production. This means that if there is shortage of a vaccine, [the purchaser] is guaranteed to get whatever cut of the available supply was paid for—the industry partner cannot go and sell the vaccine to somebody else who is willing to pay more.

How are vaccine prices negotiated?
It's an open, competitive process among the manufacturers.

Is the process different for new vaccines which have not yet recouped development costs?
The process is similar, although the prices would be higher. Whether this will stay the same in the future or not is a topic for more discussion among the manufacturers and purchasers.

What practical advice do you have for AIDS vaccine stakeholders who are thinking ahead to possible procurement schemes?
You need to define the specific countries for which your reduced price procurement is valid. We have defined it as the world's poorest countries, and we then say to industry, "We are not going to interfere with the prices of this vaccine in middle or higher income countries." We are not trying to set a price standard for these other markets—we've explicitly agreed to segmented markets at different prices.

How do you think a future AIDS vaccine be financed?
The Vaccine Fund is seen by donors as the global commodity financing mechanism for vaccines. We have learned from vaccine procurement so far that it is advantageous to have a single mechanism for securing the desired products at the best prices in a timely fashion.

Will GAVI play a role in distributing an AIDS vaccine?
We see the most strategic role for GAVI as preparing the ground for a future AIDS vaccine. Countries need to strengthen their health systems today to ensure rapid delivery of an AIDS vaccine as soon as one becomes available. And the global community needs to be convinced of the high value of vaccines in general, so they will commit the necessary resources for development and eventual purchase of an AIDS vaccine.

Finally, GAVI is focused on the development and introduction of new technologies that will improve access to vaccines—such as reduced reliance on the cold chain and, ultimately, eliminating the use of sharps.

Are there efforts underway to help countries make plans for how they will sustain GAVI-funded vaccination programs after their five-year grant ends?
After five years GAVI and the VF would like to move on to finance new vaccines that come on the horizon, including an AIDS vaccine. So it is important that countries take on the financing for basic vaccines now covered by GAVI. We have guidelines for countries on how to develop sustainability plans.

One thing we try to do is to link countries' immunization needs into broader initiatives like poverty reduction strategies. For example, in Tanzania, the budget for immunization is being tripled over the next 2 years, thanks to a link with a poverty reduction strategy that includes immunization coverage as an indicator.

Have there been changes for GAVI since 9/11, for example, in the arguments you make, or the questions you need to answer?
Yes, 9/11 has meant some changes for the vaccine field. One is that there is now development of vaccines against bioterror. This can threaten some of the capacity for producing routine vaccines. I think it is only limited competition, but it has been flagged as a potential concern.

The second point is that eradication goals have been weakened. I think the possible reintroduction of smallpox vaccination will influence decision-making, for example about polio—there are increasingly arguments that we should continue to vaccinate, even after polio has been eradicated—or about whether we should go for measles eradication.

On the other hand, all this opens up new opportunities for technology development, and for the delivery of vaccines.

GAVI is working on two projects that will create resources for the field—an immunization financing database and a "Lessons Learned" study. Can you describe these projects?

The idea behind the Lessons Learned study is that we want to gather the lessons from each individual step. For example, we want to learn from the first procurement round so we can do better in the next round, which is coming up next year.

The Lessons Learned study also provides more detailed information about the vaccine industry, including earnings, markets, and activities of producers in the North and South. We had only a study from 1993 to build on. So it was important to get updated.

The immunization financing database will be an important guide to what we can ask in terms of country-level and international support for immunization programs. And it will be helpful to show how we fare in relation to mobilizing general support for immunization services.

How is GAVI working with the Global Fund to Fight AIDS, Tuberculosis and Malaria?

We have been participating closely in the development of the Global Fund, though not everything we proposed has taken hold.

We suggested that it would be good to have a defined number of countries. But that was not accepted. Another suggestion was to have clearly defined criteria as a baseline against which to measure progress. And we proposed that there be a short list of basic indicators like those developed by other programs, such as UNAIDS, Roll Back Malaria or StopTB. That was not approved either. I think this will be a challenge to the Fund—they want to be performance-based, but they didn't make the hard decisions needed to actually make it performance-based. But with Richard Feachem on board [*as the Fund's new head*], I'm sure things will change.

How important is political will in the work that GAVI does?

One of the gratifying things about the whole process has been the political commitment, both in the North and in developing countries. It's amazing. Vaccines are now seen as something like water and sanitation—they should be available to everybody. ◆

◀ **NEUTRALIZING ANTIBODY CONSORTIUM** *continued from 1*

cells to replicate—from infecting the body. It's widely believed that these immune responses will be crucial to vaccines that prevent the establishment of HIV infection.

The NAC will intensify efforts to induce these responses and to identify NAb-inducing immunogens that can be used either independently or together with the current generation of AIDS vaccines, which stimulate HIV-specific cell-mediated immune responses (including CD4 and CD8 T-cells). These responses target cells that are already infected with HIV, and in macaques can prevent or delay disease but cannot completely block infection. For this reason, many researchers are convinced that the most effective AIDS vaccines will need to induce both cellular and antibody-based (humoral) immunity.

So far, the AIDS vaccine field has yet to realize the goal of inducing broad NAbs. One obstacle is the rapid rate of mutation in the HIV envelope, which contains key NAb binding sites, allowing the virus to evolve away from potential NAbs. The envelope's three-dimensional structure also thwarts NAb binding through a complex folding that tucks key regions deep inside the protein, underneath a thick outer coating of sugar molecules.

"With the NAC, IAVI has committed to a five-year, multimillion dollar effort," says Wayne Koff, IAVI's Vice President for Research and Development. "The NAC will help ensure that an all-out effort is made to solve the problem of designing immunogens that can stimulate NAbs against HIV." Funds will be used for research in two broad categories: structural biology and immunogen design. Projects will focus on elucidating the detailed 3-D structure of the envelope protein and understanding the structure of complexes formed when HIV binds to the surface of CD4 target cells. Based on knowledge gained from these studies, the NAC will then design immunogens aimed at generating NAbs in a vaccine strategy. "The unique aspect of the NAC is its linkage of leading labs working on this problem in a way that allows flexible use of resources," says Koff. "We will try whatever it takes to solve this problem."

NAC intellectual property agreements will provide IAVI with the option of a license to develop any potential products from the consortium, to fulfill IAVI's mission of ensuring that developing countries can access successfully licensed vaccines at reasonable cost. ◆

vaccine BRIEFS

US Congress Proposes Major Increase in Funds for Global AIDS

In June, the Foreign Relations Committee of the US Senate passed legislation authorizing significantly more spending by the US government on HIV/AIDS programs in developing countries. The bill authorizes US$2.1 billion in US spending on HIV/AIDS, tuberculosis and malaria in the next fiscal year (FY2003), which includes about $1.5 billion on HIV/AIDS, and over $2.5 billion for the three diseases ($1.8 billion for HIV/AIDS) in FY2004. US spending on AIDS programs in developing countries this fiscal year is $988 million.

The bill also requires the Administration to draft a 5-year strategic plan for addressing global AIDS, including plans for broadening access to AIDS vaccines once they are available. It also calls for increased US support for IAVI (from $10 million now to $12 million in FY2003 and $15 million in FY2004). Chief sponsors of the legislation include long-time champions of HIV/AIDS vaccine research, Sens. John Kerry and Bill Frist. Majority Leader Tom Daschle is a co-sponsor.

At press time, the full Senate had not taken up the bill, although it was reported to be on a fast track for consideration. Passage by the full Senate is expected, at which point the bill must be reconciled with a somewhat different House version passed in December 2001, and then fully funded. The chief sponsor of the House legislation, Rep. Henry Hyde, welcomed the Senate bill when it was introduced this spring.

On 20 June, President Bush announced an initiative to spend $500 million over three years to reduce mother-to-child transmission of HIV. The proposed spending includes $200 million recently approved by Congress in an emergency supplemental spending bill for FY2002. The remainder must be approved by Congress. The program will be focused on 12 countries in Africa and the Caribbean.

AIDS Vaccine Delivery Forum Held at African Economic Summit

On 5 June, IAVI and the Global Health Initiative (GHI) of the World Economic Forum co-organized a forum on AIDS vaccine delivery at the African Economic Summit 2002 in Durban, South Africa. The forum featured a case-study adapted from the WEF summit in New York in February 2002 (see *IAVI Report*, March/April 2002) and was attended by over 30 people, including Njongonkulu Ndungane, Anglican Archbishop of Cape Town, and the South African minister of health Manto Tshabalala-Msimang.

Seth Berkley, IAVI President, Tore Godal, Executive Secretary of the Global Alliance for Vaccines and Immunizations (see Interview, p.10), and Helen Rees, Executive Director of the University of Witwatersrand, acted as discussion leaders for a 2-hour session that examined the needs and concerns of African industry leaders around preparing for the manufacture and eventual delivery of an AIDS vaccine. Godal urged pharmaceutical companies in the developing world to build capacity to manufacture already-licensed vaccines, which would benefit their countries and help build manufacturing expertise before an AIDS vaccine is approved.

IAVI and GHI will hold a similar forum at the Indian regional WEF meeting in November, and regional participants will report back at the annual WEF meeting in Davos, Switzerland in 2003.

AAVP Launches Program at International Gathering

On 3-4 June more than 100 of Africa's top scientists and policymakers, as well as representatives from donor organizations and the international scientific community gathered in Cape Town, South Africa for an expanded launch of the African AIDS Vaccine Programme (AAVP; see *IAVI Report*, March/April 2002). At the meeting, AAVP announced that it was seeking US$233 million over seven years to accelerate research, development and testing of AIDS vaccines on the African continent. In response, the 15 countries of ECOWAS (Economic Community of West African States) each announced pledges of $50,000 a year for 2 years.

The funds will be used to support work by partners already active on the continent, especially in preparing for clinical trials. Emphasis will go to training personnel and strengthening laboratory infrastructure and ethical and regulatory frameworks. The programme's strategic milestones call for Africa to host four Phase I/II trials by 2005 (including those already ongoing), completion of an African Phase III by 2009 and generation of plans by 2008 for assuring availability of future vaccines in Africa.

Awa Coll-Seck, Senegal's Minister of Health and Manto Tshabalala-Msimang, South Africa's Minister of Health, were guests of honor.

AVAC Releases Report on State of AIDS Vaccine Development

On 17 May, the AIDS Vaccine Advocacy Coalition (AVAC) released its fifth annual report on the state of global AIDS vaccine development since President Clinton's 1997 declaration of an AIDS vaccine by 2007 as a national goal.

"*Five Years & Counting: Science, Urgency, and Courage*" charts the past year's progress and setbacks, and looks ahead to the next steps. The report advocates expanding efforts to move diverse types of vaccine candidates into clinical trials and to accelerate clinical testing—for example, through trials that combine aspects of Phase II and III studies and might hint at efficacy prior to a full Phase III trial, and streamlining regulatory procedures for approving trials and licensing vaccines. AVAC also calls for increased funding for trials, and more support by and to communities where trials are planned.

At the same time, AVAC announced the creation of The AVAC Fund to provide small-scale emergency funds for clinical sites and communities involved with trials, especially in developing countries. The grants (with a maximum of US$2,000 each) are intended for expenses such as medical or lab supplies that are commonly under-budgeted. AVAC will begin accepting applications once The Fund has raised $10,000 (see www.avac.org for information on donating).

In the wake of 9/11, as $1.7 billion was swiftly dedicated to defense against bioterrorism, "*Five Years*" urges amplified public pressure—even outrage—to be exerted on government, industry and ourselves to ensure that momentum and focus in the search for an AIDS vaccine are not lost.

◀**INDIA UPDATE** *continued from 5*

a state of complacency, lulled by the international attention and initial success [of our programs]," he said. And he added that "there is no place for such complacency:" infection rates among injecting drug users remain high, there is continuing discrimination against people living with HIV/AIDS (especially in employment) and children of HIV-positive parents, casual sex seems to be increasingly common, and HIV is no longer the government's top priority.

Uganda, another country widely touted for its successes in AIDS prevention, was discussed by two speakers (David Apuuli of the Ugandan AIDS Commission and Alex Coutinho of The AIDS Service Organization, Uganda's largest AIDS NGO). They described the consistent leadership from government and church in HIV/AIDS awareness and prevention campaigns that helped reduce prevalence rates from double-digit numbers to the present level of 6%. Social marketing for condoms and universal primary school education have also been key elements of the national response, as have the commitment of media (100 radio stations now help spread HIV/AIDS information) and of roughly 200 NGOs working on HIV/AIDS. They also outlined some big challenges ahead: an urgent need to decentralize support systems and thereby improve facilities for care and treatment; a need to mobilize internal resources (70% of Uganda's HIV programs are funded by outside donors); increasing involvement of the private sector; and battling a growing complacency among youth.

Coutinho also pointed out that Uganda's prevention successes came on the heels of an epidemic that reached such high levels of HIV prevalence that few families have been untouched by AIDS deaths. And he urged countries which still have low infection rates to mount an early, aggressive response or risk paying the price of delay in human lives. He also emphasized that government and NGO's have worked closely together in Uganda, which has helped NGO's have far more impact.

Dirceu Greco, a clinical AIDS researcher from the University of Minas Gerais in Brazil (and member of the National AIDS Vaccine Committee), spoke about his country's experiences with both AIDS vaccines and treatment. Strong government leadership, early involvement with vaccines and a Presidential decree mandating that ARVs (including many generics produced in Brazil) are made available without charge through the public health system, have been Brazil's strengths against HIV/AIDS. There has also been strong civil society participation at all levels of decision-making, as well as solid partnerships among scientists, health professionals, NGOs and HIV-positive individuals. Greco sees Brazil's biggest challenges today as battling high rates of new infections in some areas, the persistence of stigma and discrimination, and a need to improve monitoring of HIV care.

Access to Future AIDS Vaccines

Meeting participants also heard a report on a policy workshop that took place the day before the main conference. Discussions there focused on identifying the key policy challenges raised by AIDS vaccine trials and by the goal of providing rapid access to an AIDS vaccine as soon as one is licensed. Participants also discussed how these challenges can be addressed and what concrete activities could be undertaken now, particularly by collaborations among developing country policymakers.

Looking to specific issues and situations that can inform the vaccine access debate, Brazil's Dirceu Greco and Bansidhar Mishra of Nepal reported on access to treatment and care in their countries. Both presentations emphasized the need for developing country leadership to start working towards access to future vaccines and highlighted links between access to treatment and access to vaccines.

The second half of the workshop focused on the role of policymakers in meeting the challenges of HIV/AIDS. Two case studies of successful collaborations were presented: (1) a report on the Asian Forum for Parliamentarians of Population and Development (AFPPD), by Shiv Khare, Executive Director; and (2) the experiences of TASO, in involving Uganda's community leaders and parliamentarians in the fight against HIV/AIDS, given by Alex Coutinho.

The Delhi Declaration

Throughout the meeting, Parliamentarians also engaged in backroom negotiations that resulted in a joint statement they dubbed "The Delhi Declaration." Signed by representatives from all participating countries, the Declaration (see p. 16) commits signatories to provide and advocate for strong leadership in fighting the AIDS epidemic, including the development of AIDS vaccines, and to build on pledges made at last year's UN General Assembly Special Session on HIV/AIDS (UNGASS). While similar in many ways to the final statement issued at UNGASS, the Delhi Declaration represents the first time that parliamentarians from developing countries have committed as a group to action on AIDS and vaccines.

To follow up on the Declaration, the participating parliamentarians (including Indian representatives of the different political parties) are making plans for an international working group that can continue the dialog and plan concrete joint activities. ◆

Subhadra Menon is editor of SANKALP*, IAVI's Indian newsletter on AIDS vaccines. She formerly covered health, science and environment as Principal Correspondent at* India Today*, India's largest selling news weekly, and has also written for* Frontline *magazine,* The Indian Express*,* Times of India*,* The Economic Times*,* New Scientist *and* Scientific American*.*

Delhi Declaration — Parliamentarians' Commitment Towards A World Without AIDS

The HIV/AIDS epidemic constitutes a global health emergency of unprecedented magnitude that impacts economic and social development worldwide and in particular the developing world. To combat this global tragedy, a comprehensive strategy is needed to focus on issues including health care, prevention, support, and treatment, within a legal framework designed to protect human rights. With 15,000 new HIV infections daily, there is no time to delay.

We, the undersigned, pledge to provide leadership and take concrete action to address the complexities and challenges presented by the epidemic, building on the UN Declaration of Commitment on HIV/AIDS and other international, regional, and national agreements.

We pledge to actively involve affected communities, including organizations of people living with HIV/ AIDS in policy formulation and implementation.

We pledge to inform, educate, communicate and develop strategies, working closely with affected communities, to promote effective AIDS prevention initiatives.

We pledge to identify and begin to address those factors that make individuals particularly vulnerable to HIV infection, including underdevelopment, poverty, illiteracy, lack of empowerment of women, and all types of sexual exploitation.

We pledge to promote social acceptance and respect for the dignity and rights of all people affected by HIV/ AIDS and to oppose all forms of stigma and discrimination.

We pledge to increase awareness and upgrade knowledge in societies inhibited by ignorance and deep-seated cultural and social prejudices.

We pledge to make every effort to provide progressively and in a sustainable manner, the highest attainable standard of treatment and care to people living with HIV/AIDS.

We pledge to support research and development of AIDS vaccines and other prevention technologies, keeping in mind the pressing needs of the developing world.

We pledge to support the acceleration of scientific progress, adhering to the highest ethical standards in the research, development, delivery, and use of prevention technologies.

We pledge to work to build infrastructure and take other measures to ensure access to and effective use of affordable, life-saving AIDS treatment and future AIDS vaccines when they become available.

We pledge to create an enabling environment and build capacity among policymakers in our respective countries, and in particular, seek to strengthen legislation and regulatory systems and procedures.

We pledge, as members of a global community, to strive for equitable distribution of essential resources needed to control the AIDS epidemic and to enhance the quality of life of people living with HIV/ AIDS.

We pledge to mobilize political commitment with peoples' representatives to propel a comprehensive response at national, regional, and global levels.

We pledge to promote collaborative efforts among governments, peoples' representatives, private industry, international agencies and nongovernmental organizations to move forward the commitments made in this Declaration.

We pledge to put in place ongoing mechanisms for the implementation, monitoring, and review of the Delhi Declaration.

This Declaration was issued at the International Policymakers Conference on HIV/AIDS, May 2002 in New Delhi.

◀ **MICROBICIDES** *continued from 4*

Informed consent, ongoing education

Barbara Friedland (Population Council) described an extensive back-and-forth with community representatives to revise the Carraguard informed consent form. Key issues: defining terms like speculum, microbicide, anal sex, and randomization in Tswana, Zulu and Xhosa, and finding ways to explain potential adverse events in cultures unused to the exhaustive consent forms used in Western medical information. The first version of the form "did too well" in cataloguing every possible side effect, however rare, Friedland noted wryly—leading participants in a pilot project on informed consent to argue that volunteers for the real study were entitled to greater compensation due to the risks involved.

Significantly, all of the trials were able to enroll women without directly involving their male partners in the informed consent process. Whether or not women in many countries have the autonomy to give independent informed consent is a looming question for trial planners, particularly in resource-poor settings where poverty and societal norms limit women's access to confidential healthcare services.

This issue becomes even more complex when dealing with adolescents. Although they are disproportionately affected by HIV—15-19 year-old females are up to five times more likely to be HIV-infected than their male counterparts in regions of sub-Saharan Africa—18 is the age at which most can legally consent to participate in scientific trials. They are also socially constrained by families and communities, who may view participation in an HIV-related study as proof of stigmatized, sexual behavior.

While vaccines and microbicides trials are both grappling with when and how to enroll adolescents, microbicides researchers may take the plunge first, since product safety profiles

may differ in this young age group. Compared with older women, the cervix of adolescents has more exposed columnar epithelium, a tissue thought to have almost no defenses against invading pathogens, and could theoretically respond differently to topical microbicides.

Regulatory agencies may also require data from adolescents (and a wide range of other women) before they will license a microbicide. Indeed, that was the message of a presentation at Antwerp by Sheena McCormack (Medical Research Council, UK), who summarized a WHO-sponsored meeting in March that discussed regulatory issues related to the approval of microbicides. "We need safety data that represents the general population, and therefore we have to include adolescents," she said. McCormack also mentioned other groups that should be included, such as HIV-positive and postmenopausal women.

Unfortunately, there are no easy solutions to the challenges of adolescent enrollment. Soon, the upcoming Phase III Carraguard trial will seek to drop the minimum age for enrollment from 18 to 16. Janneke Van de Wijgert (Population Council), a principal investigator on the trial, says that they are working with each local Institutional Review Board (IRB) to determine whether 16-year olds will be allowed to enroll, with or without parental consent, and that the trial will seek parental consent where needed. At two participating sites in Botswana, feedback from focus groups suggests that adolescents at these sites are unlikely to get (or seek) consent from parents, who do not want to believe that their children are sexually active, says CDC study coordinator Dawn Smith. To circumvent this, Smith says the team may recruit teenage girls who have just given birth (25% of whom are HIV-positive)—since their parents will know that they're sexually active.

Other presentations in Antwerp underscored the difficult truth that people in the hardest hit areas may approach experimental microbicides with false hopes engendered by desperation. For example, Lut Van Damme (Institute for Tropical Medicine, Antwerp) presented a COL-1492 sub-study on beliefs of participants from Thailand, Western and Southern Africa. In South Africa, the epicenter of the AIDS epidemic, 56% of participating women said that protection from HIV was the most important characteristic of the experimental product. This figure dropped—roughly in keeping with HIV prevalence in the regions—to 22.5% in West Africa, and 7.8% in Thailand. Instead, some of these participants emphasized the gel's lubricant qualities and perceived enhancement of vaginal "cleanliness" as the main benefits of the product.

Van Damme's colleague Ethel Quana (Medical Research Council, South Africa) followed with results of 15 focus group discussions and 103 interviews conducted with South African sex workers 12-15 months after the COL-1492 trial ended. Many of those interviewed said that they believed the product protected them from STDs—even when not using condoms and when their clients reported having STDs. "Despite provision of information [at monthly clinic visits], participants retained false perceptions of the product," Quana noted.

CDC's Dawn Smith says she's seen a similar tendency to believe that microbicides are effective in focus groups in Botswana. "We'll start out by explaining that we don't know whether the compound works. And within 10 to 15 minutes, the group starts talking as if it does work. It's very, very scary," says Smith.

Dealing with Failure

The microbicides field has already had to learn the hard way how to absorb the impact of an efficacy trial that doesn't deliver positive results—in this case, COL-1492, the pivotal trial which found that commercial sex workers who used N-9 as a vaginal microbicide had a slight but significant increase in risk of HIV infection as compared to those who used a placebo gel. This is thought to be due at least partly to micro-tears and irritation of the vagina caused by prolonged use of N-9 as a topical microbicide. These data were first presented in 2000 at the International AIDS Conference in Durban. But as multiple presentations and a special symposium in Antwerp illustrated, the field is still examining how to absorb the trial's lessons and find better ways to evaluate microbicide safety pre-clinically.

The good news: many sites which had been on the starting line for a follow-up study of N-9 (in a film formulation called Conceptrol) were able to switch course in midstream and launch other studies, such as acceptability studies of dummy gels, or condom-use protocols. Field leaders said that, for the most part, the COL-1492 results did not have a significant negative impact on microbicide trial plans, perhaps because N-9 was already an approved product--so the data, while disappointing, did not reflect badly on the field's overall development.

On a more cautionary note, counselors and care providers reported anger and frustration on their part, and that of their clients, over the shift in messages—now having to tell women not to use N-9 as a lubricant during sex. As one South African counselor pointed out in Antwerp, "We're concerned about recommending another product and then having 'something happen' and we have to come up with new messages again."

Defining standards and care

The most emotional session discussed standard of care for participants and communities. This is also a difficult topic in the vaccine field, where most of the discussion revolves around whether (and how) to provide antiretroviral medications for volunteers who

continued on 18 ▶

◀**MICROBICIDES** *continued from 17*

become HIV-positive during a trial. But, as presenters at Antwerp emphasized, many microbicide trials will take place in settings where providing even the most basic health care services may be a strong inducement for people to enroll in a research study.

Comments from participants in the Phase II Carraguard trial offer dramatic support for this view. Some were so pleased with their care—including Pap smears, GYN exams and STD treatment—that they asked to enroll in the upcoming Phase III study. This posed a challenge to planners who wanted to randomize unbiased participants, but did not want to alienate the community by excluding these eager trial veterans. Ultimately, the decision was made to allow Phase II participants to enroll, but to avoid seeking them out.

Another vivid report from the field came from Cameroon's Leopold Zekeng, whose microbicide trial provided treatment for STDs and vaginal infections. "In situations where women were clear of STDs, we thought they would be happy," Zekeng reported. Instead, "They were unhappy because they were not getting drugs that others were getting." Having never been in a situation where pills were readily dispensed, women wanted to benefit fully, he said. In this case, the researchers decided to give out vitamins to women who did not have STDs.

These problems will only increase as trials get larger, said South Africa's Coetzee. Guguletu has a 20% HIV prevalence rate. "During the screening process, we'll uncover high numbers of HIV-positive well women and a lot of women with abnormal Paps who will flow into existing health services. We're going to need to think about how the community will benefit from and access health care services while we're doing the trials."

Sharing fertile common ground

One of the most striking things about the Antwerp meeting, according to some participants, was the attention given to overlaps between AIDS vaccines and microbicides. Peggy Johnston, Assistant Director for HIV/AIDS Vaccines at the U.S. National Institute of Allergy and Infectious Diseases (NIAID), gave a plenary lecture on "Analogies Between Research on AIDS Vaccines and Microbicides;" later in the week, Lori Heise, head of the Global Campaign for Microbicides, delivered a thought-provoking talk comparing advocacy for AIDS vaccines, microbicides and treatment.

These comparisons are being borne out in the field, where there's more overlap than ever between prevention and treatment, and between vaccines and microbicides. Hlabisa, South Africa is a prime example. This very high-incidence area was the site of extensive community education and mobilization during several years of NIH-sponsored preparedness for Phase III vaccine trials—which are still at least several years away.

This gap has led Hlabisa to move into microbicides trials. In July 2002, the South African Medical Research Council (MRC) and NIH-sponsored HIV Prevention Trials Network (HPTN) will launch a 150-woman feasibility study to lay the groundwork for Hlabisa's participation in a microbicide trial (HPTN 035), where it will enroll 1000 women. "We've spoken truthfully with the community and they understand that there will not be a vaccine for a while," says MRC's Gita Ramjee. "So we are going to do a microbicide trial."

There may also be joint action on policy fronts, as both fields seek to maintain and strengthen the demand for products which do not yet exist, and which may still be years away—even the most optimistic estimates say it will be five years before the first microbicide is approved.

As those gathered in Antwerp agreed, both AIDS vaccines and microbicides will continue to be propelled by the forces that have carried them so far: a mixture of optimism, perseverance and accumulating knowledge. Peggy Johnston was one of several speakers who grappled with the question of how to rally politicians—many of whom have a short tenure in office—to support products that may be years down the road. In answer, she reminded the audience that, centuries ago, cathedral building was thought to be a most noble profession—and that the laborers who worked on them did not know if they would be completed in their lifetime. Johnston urged the crowd to share this message with potential political and private sector allies. "Let this be our cathedral," she said. ◆

◀**BARCELONA 2002** *continued from 2*

Turning to the broader vaccine landscape, we speak with Tore Godal of the Global Alliance on Vaccines and Immunization (GAVI). Godal discusses some of GAVI's "lessons learned" from its first round of funding programs to vaccinate more children in the world's poorest countries against basic childhood diseases. And he describes the emerging political commitment across the world to make these vaccines available to all.

The search for an AIDS vaccine is proving to be long and frustrating. Success will take vision, scientific breakthroughs and mobilization of far more resources than are now available. But perhaps at the International AIDS Conference in Bangkok 2004, we will look back on Barcelona as the event that catalyzed a new level of funding and commitment, in keeping with the scale of the epidemic. ◆

◀IDUs AND HIV VACCINES *continued from 8*

may make it difficult to analyze the influence of transmission route on vaccine-induced protection in this group.

WHERE COULD VACCINE TRIALS IN IDU BE DONE?

In addition to Bangkok, where there is hard evidence that IDU can be enrolled and retained, there are several other IDU cohorts which could participate in future trials. Also in Thailand, a cohort in Chiang Mai supported by the National Institute of Drug Abuse (NIDA, the NIH institute focused primarily on substance abuse), led by David Celentano and Vinai Suriyanon, found a high, steady seroincidence among 400 IDU of 7.7/100PY (95% confidence interval 5.0-10.4) despite risk reduction counseling, condom promotion, and training in safe injection practices. Virtually all newly infected IDU in this cohort have the same HIV subtype E found in cohorts at sexual risk in Chiang Mai.

Several sites are now being built up in China. The HVTN is supporting a site in Guangxi Province (southern China) together with the HIV Prevention Trials Network (HPTN), which also works in Xinjiang, in China's far northwest. Both sites are involved in HPTN 039, a cohort development study aimed at assessing retention, seroincidence, and cohort capacity. The same protocol is also underway among IDU in St. Petersburg, Russia, and among IDU in Philadelphia, also with HPTN support.

Elsewhere, a clinical trial in New Delhi, India is testing whether new drug treatments for addiction are a useful HIV prevention tool. The study is a collaboration between SHARAN, an Indian NGO that works with drug users in the city's slum districts, and researchers at Johns Hopkins, and is supported by NIDA as a possible vaccine trial platform. Groups in Philadelphia and Baltimore have demonstrated high retention and, in Baltimore, sustained seroincidence among young injectors. Other studies involving HIV in IDU are underway in Hanoi, Moscow, Karachi, and several Brazilian cities.

If an HIV vaccine is to help turn the tide against HIV/AIDS, it must be effective against IDU transmission. With appropriate commitment and buildup, IDU cohorts suitable for these trials can be available. Engaging them, in turn, requires expanding partnerships with drug users, NGOs and research groups active with IDU, and the vaccine research community. ◆

Chris Beyrer is associate research professor of epidemiology at the Bloomberg School of Public Health of Johns Hopkins University in Baltimore and a Senior Scientific Liaison for the HIV Vaccine Trials Network. From 1992 to 1997 he served as field director for vaccine preparedness studies (PAVE and HIVNET) at Chiang Mai University, also gathering material for his 1998 book, War in the Blood: Sex, Politics, and AIDS in Southeast Asia. *He has retained close ties to the region as subunit principal investigator of the Chiang Mai HVTN trial site and investigator in China and Laos.*

IAVI is calling for nominations for a new Policy Advisory Committee to help guide IAVI's board and staff on our policy program. This program is aimed at identifying the policy actions at the international and national level necessary to accelerate the development of an AIDS vaccine and to ensure swift global access once a vaccine is available. IAVI is looking for experts in various areas, including global health policy; procurement and delivery systems for vaccines; regulatory issues; economics of vaccines ;private sector vaccine development and manufacturing; and international financial mechanisms. For more information about applying or nominating candidates, please see IAVI's website (www.iavi.org,) or contact Lydia Williams, Policy Director, IAVI, 212-847-1052 or lwilliams@iavi.org.

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The *IAVI Report* is published bi-monthly by the International AIDS Vaccine Initiative. To obtain a subscription to the *IAVI Report*, or for reprint permission, send name, address and request by e-mail to: iavireport@iavi.org; by fax to: 1-212-847-1112; by mail: IAVI, 110 William Street, 27th floor, New York, NY 10038, USA.

iavi International AIDS Vaccine Initiative

IAVI is a scientific organization founded in 1996 whose mission is to ensure the development of safe, effective, accessible, preventive HIV vaccines for use throughout the world. IAVI focuses on four key areas: accelerating scientific progress; education and advocacy; ensuring vaccine access and creating a more supportive environment for industrial involvement in HIV vaccine development.

IAVI is a UNAIDS Collaborating Centre. Its supporters include the Rockefeller, Alfred P. Sloan, Starr, Bill & Melinda Gates, Until There's A Cure and John & Marcia Goldman Foundations; the governments of the United Kingdom, The Netherlands, Canada, Ireland, Denmark, Norway and the United States; and the Mercury Phoenix Trust, World Bank, UNAIDS, National AIDS Trust, New York Community Trust and Fondation Marcel Mérieux. IAVI has also received support from Crusaid, the Elton John AIDS Foundation, the Vincent P. Belotsky, Jr. Foundation, Levi Strauss International, and other generous corporate and individual donors around the world.

Vaccines at Barcelona

DATE/TIME/TOPIC	VENUE
FRIDAY, 5 JULY 2002	
9:00 – 18:00	
Canadian HIV/AIDS Legal Network Co-Sponsored Satellite session: *Vaccines, Access to Treatment and the Law*	Barceló Hotel Sants, Plaça dels Països Catalans, Barcelona
SATURDAY, 6 JULY 2002	
9:00 – 17:00	
IAVI Co-Sponsored Satellite session: *AIDS Vaccines for the World*	Hotel Arts, Carrer de la Marina 19-21
SUNDAY, 7 JULY 2002	
9:00 – 12:00	
ORVACS Satellite Symposium session: *Therapeutic Vaccination for HIV Infection: The Future*	Hall 2:5
11:30 – 13:15	
International AIDS Women's Caucus Satellite session: *Women and Prevention Panel (featuring IAVI speakers) at "HIV and Women's Lives post-UNGASS: Science and Activism Joining Forces"* (8:30 – 16:30)	Conference Center
MONDAY, 8 JULY 2002	
12:00 – 13:30	
Poster presentation:** *HIV Vaccines*	Palacio 4 – A corner
14:00 – 15:30	
Oral abstract session: *Humoral Immunity to HIV*	Hall 1:1
16:00 – 17:30	
Oral abstract session: *Vaccines I*	Hall 1:1
16:00 – 17:30	
Bridging session: *Opportunities and Challenges in Vaccine Research and Development*	Hall 1:2
Poster sessions* • *New Approaches in HIV Vaccines* • *Vaccine Development* • *Phase III Vaccine Trials*	Poster hall
TUESDAY, 9 JULY 2002	
8:55 – 9:15	
Plenary session: *HIV Preventive Vaccines: Science and Politics*	Palau St. Jordi
10:00 – 11:00	
Press briefing: *IAVI announces the formation of the HIV Neutralizing Antibody Consortium*	Barcelona Two, Media Center
11:00 – 13:00	
Offsite Community Event: *Women and AIDS Vaccines: An Interactive Discussion of Important Issues (moderated by IAVI)*	Community Cultural Center, Montalegre No. 7 (*for directions*: www.womenatbarcelona.net)
16:00 – 17:30	
Oral abstract session: *Vaccines: Preclinical to Clinical*	Hall 1:1
Poster sessions • *Preventive HIV Vaccines: Advancing Global Research and Future Access* • *Development of Next-Generation AIDS Vaccines Based on Sequence Analysis of gp120 Variation in the AIDSVAX® North American Phase III Clinical Trial*	Poster hall
WEDNESDAY, 10 JULY 2002	
10:30 – 12:00	
Symposium session: *Vaccine Trials*	Hall Verdi
10:30 – 12:00	
Symposium session: *Immune Response to HIV*	Hall 2:4
12:30 – 13:30	
Poster presentation: *Vaccine Trials*	Palacio 4 – D corner
14:00 – 15:30	
Symposium session: *New Hope for an HIV Vaccine*	Hall 1:1
Poster session: *Phase I/II Trials*	Poster hall
THURSDAY, 11 JULY 2002	
18:00 – 20:00	
AIDS Vaccine Advocacy Coalition (AVAC) Satellite session: *Vaccine Community Meeting*	Room 2.B
Poster session: *Humoral Immunity*	Poster hall

**Posters are on display all day; authors are available for questions 12:00 – 14:00 (Monday – Thursday).*
***Poster presentations are short talks by featured poster authors.*

IAVI BOOTH — Main exhibition hall, stand A49