July 2005 • Vol.3 • No.7

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BULLETIN ON AIDS VACCINES • WWW.IAVIREPORT.ORG

Spotlight

Brazil's leadership on AIDS: Acting in the present while preparing for the future

Brazil's sprawling and geographically diverse landscape is home to the world's fifth largest population. Ten years ago it was also home to an exploding AIDS epidemic. The number of HIV infections was soaring, mainly among injection drug users, sex workers, and homosexual men. But Brazilian society's open and direct attitude towards sexuality, a characteristic that was suspected to fuel the spread of HIV, also allowed the country to organize a broad and effective response to AIDS. Now the country is widely regarded as a model for HIV prevention and treatment in developing countries.

Rather than rest on its laurels, the Brazilian government continues taking bold strides in the fight against AIDS. Despite pressure from richer countries, the Ministry of Health recently accelerated the move towards producing newer antiretrovirals (ARVs) at a considerably lower price in order to secure access to the best drugs for all in need. The country's AIDS program also recently rejected a large grant from the US because of ideological restraints that would have jeopardized the nation's prevention programs. Yet even with such strong political will, healthcare workers who are administering treatment and prevention programs still struggle to maintain quality care.

Brazil's success is rooted in the ability of the healthcare sector to balance access to treatment with a continued emphasis on prevention. "Treatment, prevention, and care are all part of the same package and each is equally important," says Pedro Chequer, the head of the National AIDS Program.

The emphasis on prevention helped pave the way for discussion about AIDS vaccines. The government gave early support to national vaccine efforts by implementing a national vaccine plan as part of the overall AIDS response. The Brazilian government and an array of non-governmental organizations (NGOs) work simultaneously for the rights of those infected with HIV as well as in preparation and advocacy for AIDS vaccine trials, illustrating the country's commitment to both short- and long-term interventions to curb the epidemic.

Making treatment for all a reality

The death rate from AIDS has been slashed in half since 1996 when the Brazilian government launched a universal treatment program that provided life-saving ARVs to all in need. The World Bank's bleak prediction that 1.2 million Brazilians would be HIV-infected by 2000 was averted. Only half that number of infections actually occurred. This year 170,000 people in Brazil will receive treatment financed by taxpayer money at a cost of around US$400 million.

According to the latest statistics from the World Health Organization and the United Nations Joint Programme on HIV/AIDS, Brazilians make up nearly 6% of the total number of people receiving ARV treatment in all low- and middle-income countries. The number of new infections has stabilized and HIV-infected people are living longer thanks to a selection of eight ARVs manufactured domestically. The government facilities that manufacture these generic (or copied) versions of ARVs were able to do so until now without violating domestic patent laws, which usually protect drugs for a set number of years after they are initially licensed. Brazilian law allows any drug licensed prior to 1997 to be manufactured as a generic, enabling cheaper production of several of the first generation of ARVs. In the years since Brazil began its national treatment program the government has negotiated lower prices with pharmaceutical companies to obtain nine of the newer ARVs that they don't produce generically. But these discounts are not enough. The government spends 80% of its annual budget for the purchase of ARVs on just a few patented drugs. The purchase of one of these drugs, lopinavir/ritonavir (Kaletra, manufactured by US-based Abbott Laboratories), is eating up almost a third of the money Brazil spends on treatment each year.

The guidelines of the World Trade Organization allow member countries like Brazil to obtain a compulsory license, or break patents, on newer medicines if it is done in the public interest, and Brazil is preparing to do just that. After pressure from Brazilian civil society groups and foreign activists, the country's health minister

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issued an ultimatum to Abbott: either lower the price of Kaletra or Brazil will produce its own generic version.

Inside Brazil this move was viewed as a necessary step to sustain the universal treatment policy in the face of escalating expenses. "We need to reduce the cost and Brazil isn't doing anything wrong by implementing international law," says Chequer. "For us it's not about business, it's about human rights."

Activists in Brazil also supported this tactic, which received heavy criticism from pharmaceutical lobbying groups in the US that argue compulsory licensing will limit the companies' return on their investment and discourage them from investing in the research and development of new ARVs. "Developing countries have to use every available legal option to ensure access to treatment," says Jorge Beloqui of Grupo de Incentivo à Vida (GIV) in Sao Paulo. "I think the government is doing the right thing." Negotiations are also ongoing on two other drugs (efavirenz and tenofovir) that Brazil purchases from multinational pharmaceutical companies.

Abbott has just recently agreed to lower the price of Kaletra, saving the government an expected $259 million over the next six years and many are pleased that the government has reached common ground with the company. "It's [compulsory licensing] a radical strategy and I think it's important to negotiate as much as possible," says Monica Barbosa, a community education coordinator at the HIV Vaccine Trials Network site in Rio de Janeiro.

On their terms

While the health minister battles for lower drug prices, the country's National AIDS Program recently made headlines for refusing millions of US dollars to fund the country's prevention programs. While this may seem a contradiction, it makes perfect sense to Chequer.

Along with the National AIDS Commission, comprised of a diverse group of scientists, politicians, and community members, Chequer decided to turn down a $40 million grant from the US Agency for International Development (USAID) because it came with a clause requiring Brazil's government program to exclude any mention of sex workers' rights. The success of the country's prevention programs has been in their ability to work closely with affected and at-risk groups like sex workers and injection drug users. This approach has been effective at avoiding some of the stigmatization that surrounds other countries' epidemics and the commission refused to risk alienating sex workers. "The most important point is not the money. It's not that we have too much money, but the way we apply it is very important and we want funding to be inclusive, not exclusive, to very important parts of our society," says Chequer. The national program is still awaiting a response from USAID to see if they will fulfill the grant without the controversial requirement.

> ***"Despite the fact that treatment is available, for us prevention is still the most important measure."***
>
> **Pedro Chequer**

Brazil's move was dubbed "bold and insightful" in an editorial by the British medical journal *The Lancet*. The editorial praises Brazil's move for sending a message to funding agencies that discrimination will not be tolerated. Sex workers sit on the National AIDS Commission and other important organizations within the Brazilian AIDS program and Chequer quickly points out that they are partners, not just constituents. "You can't exclude our partners or reject their rights," he adds. However, many other developing countries that depend largely on US aid are not in a position to make such a bold move.

Brazil's independence is a result of a strong political and financial commitment towards AIDS. From the start Beloqui and his fellow activists argued that access to treatment and prevention was a basic human right for AIDS, just as it is for any disease. But Brazil did have to overcome some ideological roadblocks of its own. It is South America's largest country and has the world's largest Roman Catholic population. The church opposed the government's AIDS efforts at the start, including the use of condoms. The government, in partnership with the country's NGOs, distributes millions of free condoms, some locally produced from factories deep in the Amazon where latex is harvested from native rubber trees. Now the church plays a critical role in the national response and church members work closely with government and civil society organizations.

Messages on AIDS vaccines

Although Brazil is hailed most often for its success in providing treatment, the country's early advocacy for the development of AIDS vaccines was another critical component of organizing a comprehensive response to the epidemic. In 1992 a National AIDS Vaccine Plan was created and three years later Brazil's first clinical trial of a preventive vaccine candidate began.

The adoption of a vaccine strategy was possible because of the activities of NGOs, who supported outreach and education from the start. Brazilian NGOs were chosen to serve on the National Committee on HIV Vaccines and they began disseminating some of the earliest information on vaccines while they were still advocating for treatment access. This involvement gave several of the groups most affected by HIV a role in the process. Beloqui, himself HIV-infected, publishes bulletins on AIDS vaccines for GIV and hosts workshops. "NGOs here don't separate prevention and treatment. I think this is the only way in countries like Brazil," says Beloqui. "We view AIDS vaccines as just a different aspect of your right to health. They are all linked together."

Preparations for vaccine trials in Brazil benefited from the health infrastructure that was established as treatment programs rolled out. Several groups of volunteers participated in research studies to determine the prevalence and incidence of HIV infection, which help lay the groundwork for planning future vaccine trials.

But to date Brazil has only hosted three preventive vaccine trials. The

most recent began in 2004 to evaluate the safety of a vaccine candidate developed by the US-based company Merck. The vaccine delivers non-infectious pieces of HIV with the help of an adenovirus vector. The trial is taking place at three sites in Rio de Janeiro and Sao Paulo. Also, a therapeutic vaccine candidate has just entered Phase II trials at sites in the northeast of the country in the city of Recife.

Barbosa argues that these vaccine activities are insufficient for a population of 180 million people and she worries that the Brazilian public does not see a vaccine as urgent now that treatment is available. "If you compare our response to other developing countries, then we live in heaven. But it's not perfect," she says. "Our vaccine initiatives are still very timid compared to the national response to AIDS." And it still remains difficult for healthcare workers to mobilize the population a round AIDS vaccines because of the small number of trials in the country.

A challenge for community-based organizations like GIV is balancing the advocacy message with caution about the scientific obstacles and potential timeline for a successful vaccine candidate. "When some people hear about trial results, they expect next year we will have it in the pharmacy," says Beloqui. Even so, he thinks Brazilians remain enthusiastic about AIDS vaccine research.

"Despite the fact that treatment is available, for us prevention is still the most important measure," adds Chequer.

Global News

WHO and UNAIDS give update on "3 by 5" treatment program

One million people in low and middle-income countries are now receiving antiretroviral (ARV) treatment, according to the latest statistics from the World Health Organization (WHO) and the United Nations Joint Programme on HIV/AIDS (UNAIDS). This represents an increase over the 400,000 on treatment when WHO launched the initiative in 2003 but falls significantly short of the goal to treat 1.6 million people by the end of June 2005.

Although WHO officials suggest that the ultimate target of treating 3 million people by the end of this year will not be met, the program is still seen as a success for expanding treatment in 152 low and middle-income countries. Stephen Lewis, the United Nations Special Envoy for HIV/AIDS in Africa, said the 3 by 5 initiative has "unleashed an irreversible momentum for treatment" and that access to treatment has emphasized the importance of prevention.

The expansion of treatment access in sub-Saharan Africa, where there is also the greatest need, has been the most dramatic. A three-fold increase in the number of people receiving ARVs occurred just in the last year.

Of the 1 million people now on treatment, 350,000 are receiving ARVs funded by the Global Fund to Fight AIDS, Tuberculosis, and Malaria or the President's Emergency Plan for AIDS Relief (PEPFAR).

Officials at WHO hope the expansion of access to ARVs will help stabilize the pandemic, which caused 3 million deaths last year alone.

Additional funding needed to reverse spread of AIDS

New estimates are that US$22 billion in funding for the prevention, treatment, and care of HIV will be necessary by 2008 to reverse the spread of AIDS in developing countries. This money is required to improve the health capacity of developing countries through building infrastructure These latest figures are from a report issued by the UNAIDS Secretariat that was released to the UNAIDS Programme Coordinating Board. The report, "Resource needs for an expanded response to AIDS in low and middle income countries", focuses on the longer-term investments that will be critical to improving the capacity of country's to handle the AIDS pandemic.

Currently only $8.3 billion is available from all funding sources for treatment and prevention programs. Increasing international resources will help recruit and train community healthcare workers, provide new and renovated health clinics and hospitals, and will help treat 75% of the 6.6 million people worldwide in need of ARVs. A key part of this response also includes providing support for orphans and vulnerable children and more than half the $22 billion would be used to implement and scale-up comprehensive prevention activities. To view this report online see www.unaids.org.

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International AIDS Vaccine Initiative

VAX is a monthly bulletin from *IAVI Report*, the newsletter on AIDS vaccine research published by the International AIDS Vaccine Initiative (IAVI). It is currently available in English, French, German, Spanish and Portuguese as a downloadable pdf file (www.iavireport.org) or an e-mail bulletin. If you would like to receive *VAX* by e-mail, please send a request including language preference to: vax@iavi.org

IAVI is a global not-for-profit organization working to speed the search for a vaccine to prevent HIV infection and AIDS. Founded in 1996 and operational in 23 countries, IAVI and its network of partners research and develop vaccine candidates. IAVI also advocates for a vaccine to be a global priority and works to assure that a future vaccine will be accessible to all who need it.

AIDS Vaccine Program at the 3rd IAS Conference on HIV Pathogenesis and Treatment in Rio de Janeiro, Brazil

Session / Venue (Format)	Time/Abstract	Title and Speaker (Country)
Monday, July 25		
Access to treatment and prevention / Sao Paulo (PI)	08:30-10:00	Pedro Chequer (Brazil)
What will it take to control the epidemic? / Rio de Janeiro (F)	14:10 MoFo0101	Reducing HIV transmission: Lessons from Rakai and other African studies Ronald Gray (US)
	14:25 MoFo0102	Modelling impact of ART on transmission Daniel Weistreich (US)
	14:45 MoFo0103	Impact of accessing methadone on the time to initiating HIV treatment among antiretroviral naïve HIV-infected injection drug users - Wood E. (Canada)
	14:55 MoFo0105	Synergy between prevention and care in Africa Marie Laga (France)
	15:15 MoFo0105	How to deal with concentrated epidemics Carlos Caceres (Peru)
Innate immunity / Manaus (F)	14:10 MoFo0401	MBL in HIV infection TBA
	14:30 MoFo0402	Importance of innate immunity in HIV pathogenesis Alan Landay (US)
	14:45 MoFo0403	NK cell function in HIV-1 infection Marcus Altfeld (US)
Clinical trials take precedent for vaccine development at the current time: yes or no? / Sao Paulo (D)	16:00 MoDe0201	Pro argument - Giuseppe Pantaleo (Switzerland)
	16:20 MoDe0202	Con argument - Dennis Burton (US)
The Global HIV/AIDS Vaccine Enterprise / Sao Paulo (SS)	18:00-20:00	TBA
Tuesday July, 26		
Prevention / Sao Paulo (PI)	08:30	Immune system prevention Sarah Rowland-Jones (UK)
	08:55	ART impact on prevention Salim Abdool Karim, (South Africa)
	09:20	Prevention host genetics Amalio Telenti (Switzerland)
HIV vaccine development trials / Rio de Janeiro (OA)	10:20 TuOa0101	Control of viremia after antiretroviral treatment and therapeutic vaccination with novel forms of DNA vaccines in chronically SIVMAC251-infected macaques - Pavlakis, G. (US)
	10:35 TuOa0102	Immune modulation in HAART-naïve, asymptomatic HIV-infected individuals undergoing therapeutic vaccination with HIV-1 whole killed vaccine - Gori, A. (Italy)
	10:50 TuOa0103	Cross clade CD8+ T cell responses in primary HIV-1 clade B infection Malhotra, U. (US)
	11:05 TuOa0104	Host genetics, viral sequence diversity and antiviral cellular and humoral immunity in HIV-1 clade B infected individuals in Peru - Zuniga, R. (Peru)
	11:20 TuOa0105	An extremely common major histocompatibility complex class I allele in Mauritian cynomolgus macaques OConnor, D. (US)
Female initiated methods of HIV Prevention / Brasilia (SS)	12:00-14:00	The Bill & Melinda Gates Foundation Speakers TBA
HIV-specific cellular immunity / Poster presentation area (PP)	12:30 TuPp0101	High degree of inter-clade cross-reactivity of HIV-1-specific T cell responses on the single peptide level Yu, X. (US)
	12:35 TuPp0102	Immunodominance and cross-recognition of CD8+ T cell responses in HIV-1-infected Chinese Walker, B.D. (US)
	12:40 TuPp0103	Duration of HIV exposure modulates the breadth and the magnitude of HIV-specific memory CD4+ T cells Trautmann, L. (Canada)
	12:45 TuPp0104	The Lysispot assay reveals HIV-specific T cells can lyse targets without secreting IFN-gamma directly ex vivo Snyder-Cappione, J.E. (US)
	12:50 TuPp0105	Evaluation of viral-specific CD8 T cell responses in HIV-1+ patients with different effect if long-term HAART Magaev, S. (Bulgaria)
	12:55 TuPp0106	Role of the thymus in HIV pathogenesis and in immune reconstitution Grossman, Z. (Israel)
Role of adaptive immunity and viral evolution in vaccine design / Manaus (F)	14:10 TuFo0401	HLA B Alleles: Influence of viral load Philip Goulder (UK)
	14:30 TuFo0402	Viral sequence diversity: Relevance in vaccine design James Mullins (US)
	14:50 TuFo0403	Immune selection of viral variants Simon Mallal (Australia)
	15:10 xxxx	Host genes that influence disease progression Gao Xiaojiang (US)
Compared to what: what is the future of HIV prevention efficacy trials? / Rio de Janeiro (D)	16:00 TuDe0101	Case Studies Ward Cates (US)
	16:15 TuDe0102	Case Studies Lynne Mofenson (US)
	16:30 TuDe0103	Discussants Cheick Tidiane Tall (Senegal)
	16:35 TuDe0104	Discussants Lori Heise (US)
	16:45 TuDe0105	Discussants TBA
Wednesday, July 27		
Planning for vaccine efficacy trials / Poster presentation area (PP)	12:30 WePp0201	Community based study of HIV-1 infection among plantation workers in Kericho, Kenya in preparation for HIV-1 vaccine trials - Foglia, G. (Kenya)
	12:35 WePp0202	Feasibility of HIV vaccine efficacy trials in South African adolescents Jaspan, H.B. (South Africa)
	12:40 WePp0203	Recruitment and retention of an HIV discordant couple cohort in Kigali, Rwanda in preparation for vaccine efficacy trials - Shutes, E. (Rwanda)
	12:45 WePp0204	Preparation for vaccine efficacy trials: baseline prevalence, estimates of incidence and demographic risk factors in populations willing to receive VCT and participate in research in Uganda and Kenya - Ketter, N. (US)
	12:50 WePp0205	Screening and enrollment in two cohort studies with different procedures and benefits in Lusaka, Zambia Ntamwemezi, J.B. (Zambia)
	12:55 WePp0206	A prospective study to estimate HIV incidence, recruitment and retention among potential volunteers for an HIV efficacy trial in Rural Uganda - Bwanika, A. (Uganda)
Therapeutic vaccination / Poster presentation area (PP)	12:30 WePp0401	Therapeutic immunization with an HIV-1 immunogen (REMUNE) induces HIV-1-specific responses against HIV-1 antigens and alloresponses against HLA-alloantigens - Fernández-Cruz, E. (Spain)
	12:35 WePp0402	Results of the Spanish phase II trial with a therapeutic vaccine: enhancement of CD4 and CD8 specific immune responses against HIV-1 antigens may allow control of viral load during antiviral drug treatment interruption in HIV-1+ individuals treated with an HIV-1 immunogen - Fernández-Cruz, E. (Spain)
	12:40 WePp0403	Treatment interruption after HIV-1 lipopeptide vaccine immunization in chronically HIV-1 infected patients. Two years follow-up - Pialoux, G. (France)
	12:45 WePp0404	Efficacy of therapeutic vaccination in combination with CpG ODN in ART-treated, chronic SIV-infected rhesus macaques - Abel, K. (US)
	12:50 WePp0405	Multi-functional effector and memory CD8+ T cells boosted by therapeutic MVA.HIVA vaccine expressing HIV-1 clade A gag in chronic HIV-1 infected individuals - Dorrell, L. (UK)
Special Lecture / Sao Paulo	16:30-17:00 WeSL01	The status of the response: what it will take to turn the epidemic around Peter Piot (Belgium)

F: session **D**: debate session **PP**: poster presentation **SS**: satellite symposium **OA**: oral abstract session **PI**: plenary session • This schedule was accurate at press time; venues and speakers may change so please check your program supplement for final details.