

October 2003

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AIDS RESEARCH

The amfAR Treatment Insider

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International AIDS
Society (IAS) Conference
on HIV Pathogenesis
and Treatment*

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A New Drug Is Hard to Find

by Elizabeth Paukstis

As much of the fanfare at this year's 2nd IAS Conference on HIV Pathogenesis and Treatment in Paris centered on appearances by Nelson Mandela and Jacques Chirac, a grim certitude was present throughout each plenary, forum and wine-tasting reception: people with HIV still need new drugs.

Indeed, one of the largest stories to break was the CATCH study, which tested 1,633 recently infected people in 17 European countries (abstract #LB1). The study found that 10% of patients were already resistant to at least one of three types of antiretrovirals. New drugs that work against drug-resistant strains are particularly in demand.

Anthony Fauci, Director of the National Institute of Allergy and Infectious Diseases, underscored these points in his keynote lecture, titled "20 Years of HIV Science." After referring to the 22 formulations and 19 drugs that have been approved for HIV, Fauci described the limitations and difficulties associated with them, concluding, "the challenges of new and better drugs are

an important part of our scientific agenda for the coming years."

Out with Old, in with Not Much New

One latebreaker session included presentations on two new drugs currently in human trials. Pedro Cahn of the Hospital Fernandez in Buenos Aires presented data on Shire's SPD754, a cytidine analog active against nucleoside-resistant isolates (abstract #LB15). In a 10-day monotherapy trial, 62 treatment-naive people took placebo or SPD754 at doses of 400, 800, 1,200 or 1,600 mg. Baseline viral loads ranged from 5,000 to 100,000 copies/mL. The biggest drop in viral load, 1.65 log, occurred in the 1,200-mg group. This difference was clinically significant compared with placebo. There were no significant changes in CD4 count, and researchers described the adverse events as mild to moderate and unrelated to the dose. The lack of CD4 response to SPD754 will warrant careful observation during longer-term studies.

The results of a study involving Tibotec's investigational protease inhibitor, TMC114, were also presented (abstract #LB16). Fifty patients who had failed two to four PI-based regimens received TMC114 boosted with ritonavir at 300/100 mg twice daily, 600/100 mg twice daily or 900/100 mg once daily. A control arm continued on its failing regimen. After 14 days, viral loads declined by 1.13 log in the 900-mg arm, 1.24 log in 300-mg arm and 1.50 log in the 600-mg arm. Adverse events, described by the investigators as mostly mild and not associated with dose, were primarily gastrointestinal or CNS-related. The company is planning a phase IIb trial.

Though these studies may be promising, they both represent drugs from classes that already contain several approved agents. So another question arose: where were data on the newer drug classes, such as integrase inhibitors and entry inhibitors?

Emilio Emini, Merck's Senior Vice President for Vaccine Research, discussed his company's development program for integrase inhibitors and vaccines at a pharmaceutical-sponsored meeting before the conference. Although he reported some encouraging results from a monkey study with L-870810, an integrase inhibitor, progress appears slow. "Preclinical observations [of L-870810] require investigation before proceeding with continued human testing," said Emini, adding that Merck had several more integrase inhibitors in the preclinical stage.

Indeed, Robert Murphy of Northwestern University in Chicago asserted that for many new drugs, it was just too early. "There's a lot of new stuff in preclinical," Murphy said, "and it's just not ready to be presented yet." Still, data from CCR5 antagonists that are being tested in humans, such as Pfizer's UK-427,857 and Schering-Plough's SCH-D, were not presented. Chris Hitchcock of Pfizer said that early phase II data on UK-427,857 would be disclosed at the Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC) in September. "We presented a lot of data last February at the Retrovirus conference. We wanted to give people a much bigger overall picture—which is what we'll do at ICAAC—and that's why we didn't present anything at the IAS meeting."

Daniel Kuritzkes from Harvard Medical School in Boston also attributed the lack of new drug data at IAS to the conference's timing. "I think this is a symptom of too frequent meetings," Kuritzkes remarked. "There were a great deal of new drug data presented at the Retrovirus conference in February, and it's been only

five months since then. I don't think this reflects a loss of momentum. Various companies are moving forward with their products, and I wouldn't have expected too much from these companies at this time."

New Info on the Newly Approved

While investigational drugs were not the conference's focus, presentations on two recently approved drugs offered a few insights. Atazanavir, approved in June 2003, was the subject of two back-to-back oral abstracts. Cal Cohen of the Community Research Initiative of New England in Boston presented data on BMS AI424-043, in which 290 people who were failing a PI regimen were randomized to unboosted atazanavir 400 mg once daily or Kaletra, plus two nucleosides (abstract #117). The 24-week results showed viral load decreases of 2.0 log for the Kaletra group and 1.7 log for the atazanavir group, a difference that was clinically significant. Atazanavir was not as effective as Kaletra, though average cholesterol levels were lower in the atazanavir arm.

But 16-week results from BMS AI424-045, presented by Bonaventura Clotet from Hospital Universitari Germans Trias I Pujol in Badalona, Spain suggest that boosting atazanavir with ritonavir improves its effectiveness without necessarily boosting cholesterol (abstract #118). In this study, 347 people took tenofovir and one nucleoside, plus either Kaletra or atazanavir boosted with ritonavir or saquinavir. Drops in viral load were 1.5 log for atazanavir/saquinavir, 1.9 log for atazanavir/ritonavir and 1.9 log for Kaletra. Both atazanavir arms had better lipid profiles than Kaletra. But it will be important to see how these results play out beyond just 16 weeks.

In a latebreaker (abstract #LB2) from David Cooper of the University of New South Wales, Australia, another newly approved drug took center stage. Cooper's presentation showed that T-20, approved in March 2003, continued its durability after 48 weeks of treatment. Past research indicated that 33% of people taking T-20 and 15% of those on an optimized background regimen had undetectable viral loads after 24 weeks. After 48 weeks, those numbers were 30% and 12%—a statistically significant difference.

The atazanavir and T-20 studies serve as reminders of how 2003 has already seen the approval of three new drugs (FTC debuted in July). The lack of phase II/III drug data at the Paris IAS conference suggests that the rate of new drug approval in 2004 may struggle to maintain the pace set in 2003.

Mother-to-Child Transmission: Beyond Birth

by Kristen Kresge

Each year over 800,000 children are infected with HIV. The source of infection: an HIV-positive parent. In South Africa alone, 100,000 children a year are born to HIV-infected mothers. Nine years after the prevention of mother-to-child transmission (MTCT) of HIV gained research prominence, an alarming number of new infections still occur.

Transmission can occur at three points: during pregnancy, birth or breast-feeding. The risk for infection ranges from 13% to 60%, depending on the population studied. Previous clinical studies, including ANRS 1201 in Africa, found that a combination of AZT and nevirapine reduced transmission rates during birth to as low as 5%. MTCT trials have made major strides in lowering risk through birth. But researchers like François Dabis—who led ANRS 1201—believe that this rate could decline further.

Current MTCT prevention concentrates mostly on post-partum transmission through breast-feeding. The 2nd IAS Conference on HIV Pathogenesis and Treatment in Paris ushered in further advances in this area and was a prime focus of the meeting.

Breast-feeding accounts for 44% of overall HIV transmission, according to Dr. Ruth Nduati, of the University of Nairobi in Kenya. The likelihood of transmitting virus through breast milk directly correlates with the mother's disease status and viral load: the higher the viral load in the bloodstream, the more virus found in breast milk. Studies have found that in HIV-infected women, 80% of breast milk samples test positive for the virus.

In richer countries, HIV-infected mothers will feed their babies formula to lower or eliminate risk of transmission. But this is not always practical in the developing world. Even in the urban centers of Uganda, where women can afford formula and have access to clean water, many still choose to breast-feed. This is due to the stigma associated with not breast-feeding, according to Dr. Pius Okong, a gynecologist from St. Francis Hospital in Kampala, Uganda. "If a mother doesn't breast-feed, it's a sign of HIV infection," said Okong. Even if formula is an option, "not everybody has the courage to use it," he added.

There may now be a safer approach for women who breast-feed, based on results of the SIMBA study

(abstract #LB7)—Stopping Infection from Mother-to-child via Breast-feeding in Africa. Clinicians gave mothers AZT and ddI, and their babies either 3TC or nevirapine, from birth until one month after breast-feeding stopped; the women breast-fed the babies for six months. Treating the babies at the same time that they received HIV-infected breast milk reduced the transmission rate to just 1%. (The study found no difference between the nevirapine and 3TC arms in the 397 children studied.) These results were strikingly lower than transmission rates in previous MTCT trials, which hovered around 15%. "If you are going to breast-feed, it's also possible to protect the baby," said Okong.

This prevention strategy requires a recommendation by the World Health Organization before it is widely practiced. But Joep Lange, current president of the IAS and lead author on the study, advises implementing the strategy immediately. "It's helpful in settings where breast-feeding is the norm," said Lange. "I recommend we get our act together and treat people who need medicine."

A major advantage to the SIMBA study's strategy was that it spared the mother from taking nevirapine, once regarded as the gold standard for preventing MTCT. Though the single non-nucleoside is by far the most convenient, and perhaps affordable, it strictly limits women's treatment options.

This is because nevirapine resistance develops quickly in the mother. In study PHPT-2, also presented at IAS, 19% of Thai women who received a single nevirapine dose during labor had resistance mutations associated with the drug (abstract #62). These included K103N, G190A and Y181C, which also confer resistance to the other non-nucleoside efavirenz. Clinicians have yet to determine how long such resistance persists, how it limits the mother's therapy options or impacts preventing transmission of HIV from the mother to her future children.

Despite the advantage of sparing nevirapine use, the SIMBA study had a few weaknesses. At delivery, the women had very mild HIV disease, with an average CD4 count of 428 and viral load of 400 copies/mL. Their mild disease status resulted from their receipt of drug therapy beginning 36 weeks into their pregnancy. Without knowing their viral loads at the time therapy was initiated, it remains unclear how effective this strategy would be in women with more established HIV infection.

Another shortcoming is the limited time that the women breast-fed—an average of three to four months—thanks to intense counseling by trial coordinators who encouraged early weaning. Whether or not this early weaning is practical or culturally acceptable outside of clinical studies is another issue.

According to Lange, the cost should not be a stumbling block to implementation. Babies received an equivalent to two bottles of medicine. “The actual price is virtually nothing. It’s extremely cheap and it’s extremely simple,” he said.

The exact price tag for this strategy may rest with GlaxoSmithKline and Bristol-Myers Squibb. It is hoped that low-cost, generic versions of their drugs might be made available. Nevirapine (Viramune) has been provided free since July 2000 by its manufacturer, Boehringer Ingelheim, in an effort to support MTCT programs in developing countries. But in fact, few have actually taken advantage of Boehringer’s offer. MTCT researchers speculate this is partly due to lack of infrastructure and getting the word out to health care workers. “It’s a lack of community mobilization around MTCT in these areas,” said Dabis, of the University of

Bourdeaux. “We need to move in the same direction at a faster pace.”

While current drug combinations are being studied, other options, such as formula feeding, are also being explored. A study from South Africa presented by Dr. David Coetzee of the University of Cape Town found that when formula was provided free to 113 women in the Western Cape, 95% chose not to breast-feed at all (abstract #220). He attributed the study’s success to focus groups that provided support for the women. But the practicality of this study is limited by the cost of formula and the incomes of the families involved. In that area, 71% of the women had fresh drinking water in their homes. This is uncommon elsewhere, and is another barrier to formula feeding.

The ultimate answer is for all women in developing countries to have continued access to anti-HIV drugs long after delivery, a missing component of most MTCT trial designs. In addition to drastically lowering transmission rates, it increases their chances of surviving long enough to care for their offspring. “Even better would be to treat the mothers,” said Lange. “Why not take the risk down to zero?”

FTC’s Approval Means One More Once-A-Day

by Kristen Kresge

Less than two weeks after the US Food and Drug Administration (FDA) approved a protease inhibitor for the treatment of HIV, another drug won marketing approval. Emtriva, also known as emtricitabine or FTC, was approved July 2 and joins the nucleoside class of existing HIV drugs.

FTC represents another step toward simpler, more forgiving HIV drug regimens. Like atazanavir (Reyataz), which was approved last month, it is a once daily therapy available as a single 200 mg capsule.

FTC, initially discovered at Emory University, was under development by Triangle Pharmaceuticals until Gilead Sciences purchased the company earlier this year. With FTC’s approval—and tenofovir’s debut in 2001—Gilead has become a major player in the anti-HIV drug market in the last two years.

FTC’s structure is akin to 3TC (lamivudine or Epivir), and a phase III trial found the potency and safety of the two drugs to be strikingly similar. In the year-long FTC-303 study, volunteers on a stable three-drug regimen containing 3TC were randomized to switch to

FTC or continue 3TC. Of the 294 patients who switched, 67% (197/294) had viral loads below 50 copies/mL, compared with 72% (105/146) of those who stayed on 3TC.

Similarities extend beyond structure. FTC’s toxicity profile appears to mirror that of 3TC, although its full safety profile is yet to be defined. Like 3TC, dosing of FTC must be adjusted for people with kidney problems, who may eliminate the drug more slowly. FTC also has activity against hepatitis B virus, so clinicians should carefully consider giving it to HIV/HBV co-infected patients.

Unfortunately, FTC’s similarity to 3TC also translates into a similar resistance profile. The major mutation that causes 3TC resistance—M184V—also causes FTC resistance. For this reason, anyone who has failed 3TC therapy would experience less benefit from FTC. This limits FTC’s potency in treatment-experienced people, where previous exposure to 3TC is common. But some studies have shown that continuing 3TC even after resistance has developed is advantageous. Although you may get a smaller reduction in viral load, these

drugs are still pulling weight, according to Dr. Michael Saag, Director of the HIV Clinic at the University of Alabama at Birmingham.

And despite FTC's comparability to 3TC, some clinicians caution against calling it a "me too" drug—implying that it offers no particular benefits over an existing drug. "Each new drug approved adds something to our ability to take care of our patients over the longer run," said Dr. Donald Abrams of San Francisco General Hospital.

FTC's distinguishing trait is its stability once in the body. After one FTC dose, drug concentration remains high for up to 38 hours, compared with 13 hours for 3TC. "Missing one [FTC] dose is probably not a major danger," said Saag. "It's a little bit more forgiving than 3TC. And with all things being equal, you may lean toward a drug with a longer half life." But Saag warned that you do not want patients missing a dose of any HIV medication.

In community meetings, Gilead representatives acknowledged that FTC's potency and resistance profile did not warrant a higher price tag than established drugs, a trend in new drug pricing. So Gilead is not expecting big profits from FTC alone. Priced at just over \$250 for a

one-month's supply, FTC comes at the same price as 3TC.

But Gilead hopes to collect blockbuster profits by co-formulating FTC and its best-selling nucleotide inhibitor, tenofovir. This single once-a-day pill could compete with the popular drug Combivir (AZT/3TC), which is taken twice daily. GlaxoSmithKline manufactures Combivir and sells it for under \$600 for a 30-day supply. Tenofovir alone sells for about \$455 a month.

Gilead expects to launch this co-formulated drug in early 2005 and is meeting with the FDA to decide on the equivalence studies needed for approval. The company has already developed a single pill containing both drugs and is confident that manufacturing will not delay availability or impact the pricing of the FTC/tenofovir combination.

A Gilead sponsored study (934) comparing FTC, tenofovir and efavirenz with Combivir and efavirenz begins enrolling this summer. Abbott is also conducting a study comparing Kaletra—taken once or twice daily—with FTC and tenofovir. The study's interim 24-week results are expected this fall. In the mean time, FTC is a simpler, but not extraordinarily unique, option in the anti-HIV armamentarium. "It's a longer acting version of 3TC," said Saag. "I'd use it the exact same way."

Brazil's AIDS Model: A Global Blueprint?

by Anne-christine d'Adesky

In June 2003, an historic agreement took place in Washington between two odd allies: US President George W. Bush and Brazil's charismatic, radical former labor leader "Lula," as Brazil's President Luiz Ignacio Lula da Silva is called at home. The duo agreed to assist in rolling out a national AIDS treatment program in two Lusophone (Portuguese-speaking) African countries, first in Mozambique, then Angola. The effort will rely on new partnerships among US, Brazilian and Lusophone African groups and institutions.

Because of Brazil's success pioneering AIDS treatment at home, it will oversee many details of these programs. That includes a transfer of technical knowledge in manufacturing generic antiretrovirals and overseeing their use in countries whose populace lacks adequate health care. The programs are part of Bush's effort to spearhead AIDS treatment to the hardest-hit nations of Africa and the Caribbean through his recently approved five-year, \$15 billion Emergency Plan for AIDS Relief.

For Brazilians, the joint agreement is the sweetest victory to date in the ongoing global effort to provide universal access to AIDS care and antiretrovirals to some 30 million people living in Africa and other developing regions.

Until now, the US has been strongly allied with big pharma in a tooth-and-nail fight with Brazilian officials to prevent generic competition in the AIDS drug arena. After failing to negotiate drug discounts from multinational patent holders, Brazil, Thailand and Cuba opted to manufacture generics.

What was at stake for big pharma wasn't really the tiny AIDS market in Africa—which represents only 1% of the billion-dollar AIDS market—but the larger patent system. Makers of new products or processes are now guaranteed a 20-year market monopoly under a WTO Agreement on Trade Related Aspects of Intellectual Property and Public Health, or TRIPs. US trade officials feared that softening TRIPs' rules for lifesaving HIV medicines in a pandemic would usher in generic competition for other products.

Undeterred, Brazil fought back, arguing that Article 68 of Brazil's 1997 patent law allowed it to make generics to address its national emergency. These drugs—made only for its national AIDS program, not for export—do not break patents. In 1990, Brazil, the second-most populous country in the Western Hemisphere, had an exploding AIDS epidemic—average survival time was less than six months after a clinical diagnosis. Most citizens lacked access to HIV tests and drugs. In 1993, the private Brazilian company Microbiologics began making generic AZT, and in 1994, the state did the same, providing AZT free through its public health system. AZT prices fell dramatically. By 1997, the government was making ddC and d4T and within two years, other nucleosides were available. In 2000, indinavir was added, then nevirapine.

Brazil's estimated savings on these last two drugs was \$80 million, or 30% of total drug costs for the year. By the time of the US WTO challenge in 2001, AIDS drug prices had fallen domestically by 70%. So had AIDS deaths. The health system had saved \$677 million, and freed up hospital beds. Armed with such positive, cost-effective results, Brazil was cast as a fiery David against the Goliath of greedy big pharma.

Four months after filing the complaint, the US dropped it. Brazil continued to up the ante, threatening compulsory licensing to negotiate sharp 40% and 65% discounts on patented antiretrovirals from Switzerland's Roche and US-based Merck. Then in November, Brazil helped broker a victory for developing countries at the 142-nation WTO Ministerial Conference in Doha, Qatar. A new ruling guaranteed poorer nations facing national emergencies the right to practice parallel importing or issue compulsory licenses to import or make generic drugs.

But the Doha agreement was only a partial victory, due to a clause banning exports and requiring countries to develop the capacity to manufacture their own generics—something they all lack. In 2002, WTO members again failed to resolve this hurdle. Although 31 countries have implemented Brazil's treatment and prevention guidelines, only Guyana has adopted its generics model. The Doha clause has effectively prevented the world from following Brazil's lead on generics.

"Why has no country adopted this? We need the agreement of countries," said Paolo Teixeira, the outspoken, outgoing head of the Brazilian Ministry of Health's AIDS program. "We can only say that some countries have tried to consider this and stopped with fear of pressure from the United States." For very poor countries, threatening to withhold foreign aid is an effective weapon.

The Pressure to Export

US opposition isn't the only reason for the global reluctance to produce generics. In reality, making quality antiretrovirals is neither cheap nor easy, even for richer countries. It requires a substantial investment, an industrial manufacturing base and technical manpower. Aside from Brazil, Thailand and Cuba's state programs, only a half-dozen private companies in India and China meet that criteria for making pills. Globally, not many can even produce the necessary raw materials. Analysts predict a few developing countries will be able to make generic antiretrovirals based on their current industrial capacity and experience. Generics are also a tough business, especially when the local market for AIDS drugs is not well established. Even when companies succeed, generic drug prices may not be cheaper than imported drugs.

In the face of these realities, there has been a growing international demand that Brazil export not just its technical know-how, but also its high quality drugs. But even with possible approval from the WTO, that won't be easy. Brazil still imports 80% of its raw materials from India, which is costly. "Many drugs could be produced in Brazil and a large number are not under patents," said Dr. Norberto Rech, head of the government technology division. Current domestic antiretroviral production, he said, "is insufficient to meet national needs."

Six of 17 public laboratories produce 15 AIDS drugs, and Brazil hopes to add four more by 2005, including two new "fixed-dose" combinations and soon, new fixed-dose drugs for tuberculosis and malaria. But it must buy 13 other antiretrovirals from private companies, nine of which are imported. A single imported brand-name drug—Viracept (nelfinavir)—eats up 27% of the current AIDS drug budget.

Brazil's own regulatory drug agency has approved the quality of its state-produced antiretrovirals. But the WHO has not conducted any quality-control inspections of the state factories or laboratories, a critical step for a drug to be included on its list of approved drugs. A WHO inspection is planned for later this year at Far Manguinhos, the state-run generics plant. Although Rech and Teixeira dismiss talk of pill exports, to an outsider it looks like Brazil is getting ready should the global call come.

"We will not break patents," insisted Teixeira. "We are focusing on the transfer of technology. Our question now is concentrated on how to solve the Doha resolution for developing countries without capacity or production. We are trying to get the WTO to adopt one resolution, for example, where Paraguay can adopt compulsory licensing and ask Brazil to produce, as a way of overcoming these barriers."

With Bush pushing his new international AIDS agenda, Teixeira said, there are hints of the US accepting such a ruling. But critics say even that revision won't do the trick, since countries would still lack political muscle to issue compulsory licenses for generic imports. In September the WTO meets again in Cancun, where a showdown is expected—along with some resolution.

While awaiting the WTO's decision, Brazil has invested \$1 million to set up 10 pilot national antiretroviral production plants, five in Latin America and the Caribbean and five in Africa. It is working closely with the WHO to develop these proof-of-concept projects. Teixeira, a tough negotiator, has also been tapped to assist the WHO's new director, Dr. Jong-Wook Lee, in the agency's goal of treating 3 million people by 2005. Teixeira began developing a global scale-up plan for AIDS prevention and care based on Brazil's model in May. In July, Lee appointed him as AIDS Program Director at WHO to implement this plan. By then Brazil was starting to transfer technology and send teams from Far Manguinhos to train technicians in Guyana and Mozambique. The new Bush-Lula agreement is part of this new era of cooperation.

"We will use this as a kind of approval of the Brazilian policy," said Teixeira of the joint US-Brazil venture. "We are putting this out publicly as a sign from the WHO, the new administration and officially the American government—after some hesitation—that they have presented their support to me. We are going to use it, because we understand it is not easy to spend this money [\$15 billion]. They will need help from WHO, from Brazil, from the NGOs (non-governmental organizations)."

Mobilizing Civil Society

With the spotlight on Brazil, the question remains: how useful is its much-vaunted AIDS model for poorer countries? After all, generics are only part of its success. Brazil's AIDS program was built upon a decentralized, unified health system that offers free drugs and care to all. It links prevention to care and treatment, and favors innovative campaigns and strategies. The government not only distributes condoms widely, but helped finance a condom factory in the Amazon rainforest using latex harvested from live rubber trees. It backs explicit safer sex campaigns in the media and has extended AIDS education to primary public schools, within a general health and sex education curriculum. Although Brazil has tough laws against illegal drug use, the government supports harm reduction and rehabilitation programs for addicts. Such progressive policies reflect a general openness in Brazilian society to subjects like sexual-

ity and hard drug use that are more taboo elsewhere. Across Brazil today, AIDS awareness is high.

According to Teixeira, the national program reflects the mobilization of a broad sector of civil society and NGOs who, from early on, viewed the AIDS battle through a civil and human rights lens. These rights are important to a society that has recently undergone re-democratization. In 1988, Brazilians ousted a 20-year military dictatorship and drafted a new constitution, then adopted their universal health care system. In 1991, universal access to anti-retrovirals began. A year later, Brazilians got rid of another president accused of dipping into the national coffers. This political engagement by gay activists and civil society spilled over to AIDS. Today, a handful of early activists, including Teixeira, hold key positions in the government AIDS programs.

"The AIDS program as a whole works very well, and I'm very supportive of that, but I always like to repeat, it is so because we were there first," explained Ezio Tavora dos Santos Filho, director of Grupo Pela Vidda (For Life), an AIDS NGO in Rio de Janeiro. An openly gay, HIV-positive activist, he can testify to a rough battle: "The community activists were there before to push the government to do something. People were dying like flies. We just hated the government. If I went to any hospital to say I had AIDS, they would put me out the door." Homophobia, activists assert, was behind Brazil's initially slow response to the epidemic, and drove them to seek legal means to address discrimination.

The role played by the church is also a bit different in Brazil than elsewhere in Latin America. Around 75% of citizens are Catholics, and many belong to a progressive wing of the church that includes radical liberation theologians dedicated to helping the poor. These religious groups have supported the government's AIDS prevention efforts, countering the opposition of a minority of conservative Catholics and evangelical Protestant groups.

An Encouraging Picture

Today, there are 600,000 Brazilians with HIV—half the number predicted a decade ago. Two hundred and fifty thousand people are under care, and 130,000 get anti-retrovirals, most of them three-drug regimens. Nationally, 70 diagnostic laboratories measure viral loads and T cells three times a year for those on therapy. Officially, anyone who tests positive and registers with the public health system qualifies for free drugs and care. The program also provides prophylactic antiretrovirals for pregnant women and health workers in case of accidental exposure to HIV.

The latest national results remain very positive, showing Brazilians with AIDS continue to benefit from therapy with quickly restored health and a return to productivity. Most patients on therapy are now treated on an outpatient basis. This has boosted their quality of life and saved the health system money.

Most also adhere well to their regimens. An April survey reported a 6.6% rate of resistance among newly diagnosed HIV cases in Brazil—far lower than similar figures for resistance in the US (15–26%), Britain (14%), Spain (23–26%) or neighboring Argentina (15.4%). Some resistance was expected in Brazil, since suboptimal AZT monotherapy and dual-nucleoside regimens were used before 1995 and 1996, when protease inhibitors were introduced. But it's good news because it shows that poverty or lack of infrastructure does not automatically spell drug resistance—something critics still cite as reasons to withhold therapy from poor countries.

On the downside, drug side effects such as lipodystrophy—a metabolic disorder that causes a disfiguring redistribution of body fat—are a growing problem. The rates are not as high as in the US or Western Europe, but still a cause for concern, said Teixeira. Yet again, Brazil has shown its humane side, helping those with severe lipodystrophy regain an appearance of health by covering the costs of facial cosmetic surgery or liposuction.

Unfinished Business

The generally rosy picture in Brazil tends to obscure the gaps. But they exist, and reflect serious hurdles. Brazil's poverty, say health officials, still limits overall health delivery, especially in rural areas. "It's very important to remember that we made a lot of progress but we didn't solve the situation absolutely," stated Teixeira. "We have some major problems concerning access and prevention. I fear they will not be solved in five years, particularly those dependent on the economic situation of the country."

Another challenge is testing. About 20% of Brazil's population has now been tested for HIV—impressive for a country of 170 million. But that still leaves four of five citizens who don't know their serostatus. The government is now pushing to increase voluntary testing rates, particularly in pregnant women; half now get tested. "That's unacceptable," admitted Teixeira.

Prisons are another problem. An estimated 15% to 20% of the total prisoner population of 200,000 is HIV positive. Conditions inside are terrible, said Teixeira, with severe overcrowding and inadequate facilities to provide care or drugs for inmates with HIV or AIDS.

Meanwhile, activists contend that universal access to care exists on paper, but reality may be different. "Officially what the government says is that everybody who needs medicine is on therapy—it's not true," said dos Santos Filho. "If you are sick and you are not in Rio or São Paulo or a major city, it will take a while to get your drugs. There is no medicine on the shelf of the pharmacy of the public health center; there is medicine for a number of people who are registered. For new cases, it can take months."

For rural residents, Brazil's vast size is a hurdle. "The only AIDS reference hospital in the state of Amazon is Manaus," stated dos Santos Filho. "We saw cases of people who had to travel 10 days to go to Manaus to get their treatment."

Finally, the health system's decentralized funding structure has its limits. It has become easier to get antiretrovirals, but not other state-funded drugs for opportunistic infections, malaria or

hepatitis. "It's very inconsistent, because the majority of the 27 states don't put a penny in," claimed dos Santos Filho. "Malaria in this country is horrible. I met people who had malaria 12 times in Manaus, a city of 4 billion people in the middle of the Amazon jungle. In February, there were 40,000 cases in an urban area."

AIDS NGOs are now beginning to work with groups fighting TB and other diseases to fill this gap. "For a long time, AIDS was seen as the rich cousin among diseases," said Ana Paola Prado of Arco Iris (Rainbow), an AIDS NGO in Brasilia. "Today, we are beginning the opposite movement—a true movement for social control of health as a whole."

Though imperfect, then, Brazil's model is a useful compass for others. Its core tenets are available to all societies: a commitment to health as a civil right, and to upholding or passing laws that protect the most vulnerable citizens from discrimination. Pro-democracy and AIDS activists, progressive church groups, bold congressional leaders and talented health officials also played important roles. "The success of the Brazilian experience is because it was built by many hands," emphasized Prado. "We do not have the best model in the world, but our model answers the demands from Brazil."

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Treatment Information Services

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