amfAR
AIDS RESEARCH

The amfAR Treatment Insider

Table of Contents

2 Nevirapine Warning — Liver Failures

3 South African AIDS Politics

5 Questions Halt Remune Trial

6 Bringing Treatment to South Africa

South Africa, HIV and the Conference

The 13th International Conference on AIDS will have commenced in Durban, South Africa by the time this issue of the *Treatment Insider* arrives in readers' hands. The biennial International Conference is taking place in a poor country for the first time. The chosen country is a nation of contradictions, with its bright European façade propped up by cheap African labor.

While well off South Africans receive modern health care, most of the country has to rely on poorly funded public clinics or traditional healers. A report on the world's health-care systems issued in June by the World Health Organization found that black South Africans pay relatively more but receive far less medical attention than their richer fellow citizens. The report rated South Africa near the bottom despite spending more per capita on health care than much more highly rated countries such as Hungary and Poland.

On top of this benighted system comes a burgeoning AIDS epidemic. By official estimates, a tenth of the total population has already contracted HIV, and that proportion is rapidly growing. As Helen Epstein describes in this issue of the *Insider*, the government has been gripped by paralysis regarding AIDS even though it holds social justice as one of its highest priorities. Instead of action, there has been endless discussion and planning, accompanied by hand-wringing over the nation's poverty.

But the nation is not so poor, and as the WHO report indicates, it spends a respectable total amount on health care. Stephen Laifer, in this issue's second article on South Africa, describes some simple steps that could make a big difference in bringing care to people with HIV. Generic versions of drugs could be manufactured cheaply in poor countries and their distribution gradually expanded from the urban, working population to the country as a whole. Brazil, with a modest epidemic but also modest health care expenditures, has led the way in this respect.

Instead of more drugs for the masses, South Africa is getting more drug trials because of the clear-cut results obtainable from its huge pool of treatment-naïve persons with HIV. Drug trials run by the international pharmaceutical industry are the only source of anti-HIV treatment for many participants, who often continue to receive drugs after completing the trial. The article on nevirapine's liver toxicities underscores the perils of this source. Drug toxicities are poorly recognized and managed even by first-rate medical systems. In South Africa, toxicity management is still more confused and can become highly politicized.

One alternative to drugs is immune-based therapies such as Jonas Salk's Remune therapeutic vaccine. In the aftermath of a trial in Thailand, the local Thai license holder is asking the government to certify the relatively cheap vaccine as first-line HIV therapy. As this *Insider* reports, Remune is engulfed in uncertainties, if not controversy, in the United States. Third World countries would do well to give rich countries' unverified therapies very careful scrutiny before rushing to embrace them.

Liver Failures Spark Nevirapine Warnings

by Dave Gilden

The South African government's Medicines Control Commission last April halted further enrollment in a trial involving the experimental nucleoside analog FTC plus nevirapine and d4T. The Ministry of Health initially blamed the nevirapine for a high rate of serious liver dysfunction and questioned the monitoring of trial participants. Seven cases of actual hepatitis, six of them in women, occurred among the 394 persons receiving nevirapine. Two of the women who contracted hepatitis died. In all, 8.6% of the trial participants experienced serious liver damage (as measured by the level of liver enzymes in the blood).

The Medicines Control Commission quickly pointed out that it is not clear which drug was at fault. An interaction between nevirapine and d4T, and perhaps all three drugs, may well have contributed to the liver problems. Still nevirapine, a nonnucleoside reverse transcriptase inhibitor metabolized by the liver, is strongly suspect. An additional 76 participants in the trial who received efavirenz rather than nevirapine had no significant liver abnormalities.

The South African ruckus over nevirapine started with a parliamentary speech by the health minister denouncing the use of nevirapine in the FTC trial. The trial was run by Quintiles Clivenpharm, a contract research organization for FTC developer Triangle Pharmaceuticals of Durham, North Carolina.

It would be easy to dismiss the controversy as emanating from the highly politicized South African debate over providing AZT and nevrapine to prevent HIV transmission from pregnant women to their babies. But almost immediately after South Africa raised its concerns over the FTC trial, the European Agency for the Evaluation of Medicinal Product (EMEA) issued its own warning about nevirapine's toxicities, The EMEA is the European Union's equivalent of the United States' FDA or South Africa's MCC.

The European agency in particular cited liver dysfunction as well as life-threatening skin rashes known as Stevens-Johnson Syndrome and toxic epidermal necrolysis. A severe constitutional allergic reaction that includes flu-like symptoms may accompany these two, the agency said, as it called for intensive, biweekly monitoring of patients during their first eight weeks on nevirapine.

Doctors should repeat the liver tests after the third month and then every three to six months. The EMEA also reminded doctors and patients to rigorously comply with instructions to start nevirapine at half-dose for a two-week lead-in period.

A doubling in European reports of nevirapine-associated hepatitis triggered the EMEA warning. Nearly all of the reported hepatitis occurred in the first eight weeks of treatment. Nevirapine's manufacturer, Boehringer Ingelheim, disputes the extent to which this increase in reporting reflects a real increase in hepatitis. Still, the company concedes that liver toxicities remain frequent.

Triangle Pharmaceuticals has proposed checking liver function weekly during the first two months if the MCC allows its trial to resume recruitment. Franck Rousseau, Triangle's Vice President for Medical Affairs, says that the two risk factors for liver problems in the company's FTC trial were female gender and skin rash. The extent of the skin rash might be underappreciated in people with dark skins, he claimed, and doctors might be inclined to "treat through" what was perceived as minor irritation not necessarily related to nevirapine.

The FTC trial was the first involving nevirapine that recruited a preponderance of women. Boehringer Ingelheim says that it will check its records to see if women are at higher risk. Nevirapine was approved in the United States four years ago, but its effects in women or blacks have yet to be fully elucidated. (Boehringer has a record of incomplete post-marketing research on nevirapine. A little over one year ago, a Yale University report caused widespread alarm when it backed up continued community criticism of the company's failure to investigate the interaction between nevirapine and methadone. That interaction requires people on methadone maintenance to have their methadone dose increased.)

Nevirapine was approved in the United States four years ago, but its effects in women or blacks have yet to be fully elucidated.

Since the first trials, it has been clear that nevirapine frequently causes liver inflammation and dysfunction. Doctors have issued occasional reports of fulminant hepatitis after starting nevirapine since the drug entered the market. This hepatitis killed at least one person in Europe during the six months preceding the EMEA warning.

In the United States, a hospital staff member this spring suffered liver failure after two weeks on AZT, 3TC and nevirapine. This health care provider, another black woman, did not even have HIV. A needle-stick accident had exposed her to HIV-containing blood, and she was taking the drugs as a preventive measure. She is alive today thanks to a liver transplant, a procedure not available to the South African FTC trial participants.

South Africa Vacillates as the Epidemic Rages

by Helen Epstein

On June 19, South Africa's Health Minister, Manto Tshabalala-Msimang launched a new five-year AIDS plan. The plan provides for broader access to HIV testing and counseling, which are now unavailable in almost half of the country's clinics. Prevention activities are a key priority, including expanded information, education and communication campaigns, continued support for vaccine research and enhanced procedures for monitoring trends in HIV and AIDS in the country. The plan also stresses the protection of the human and legal rights of people affected by HIV, especially workers and children.

Another goal is improved care for people with AIDS, including the treatment of opportunistic infections at the primary health-care level. Access to antiretroviral drugs remains a nettlesome topic since no new money is being budgeted for this or any of the other programs. Many South African AIDS experts and activists still question the government's commitment to fighting the epidemic.

Flirting with Denial

South Africa has the fastest growing epidemic of HIV in the world. The Ministry of Health estimates that 4.2 million South Africans carry the virus, and about 1,700 more people are infected every day. Those most at risk are poor black people, particularly those who have been socially displaced, such as migrant workers, truck drivers, sex workers and miners from rural areas and their wives, girlfriends and children back home.

Last fall, President Thabo Mbeki began to solicit the opinions of an obscure group of Northern scientists and activists, including University of California Berkeley professor Peter Duesberg. This group believes that AIDS is not caused by HIV but rather by a vague collection of environmental factors such as malnutrition, chemical pollution, recreational drugs and the very antiretroviral drugs used to suppress HIV. The AIDS "denialists" may not agree about what actually causes AIDS, but most seem to believe that the tens of thousands of scientists who work on HIV and AIDS are, unwittingly perhaps, part of an industry-led conspiracy to justify the multibillion dollar market in antiretroviral drugs. This conspiracy, the AIDS denialists say, relies on the demonization of HIV, a harmless virus in their eyes, and the promotion of wildly expensive, toxic drugs that have life-threatening side effects.

Many people were surprised when President Mbeki began expressing interest in their ideas. Their surprise increased in May, when Mbeki appointed a new international panel to outline an "African" response to the AIDS epidemic. The panel was divided half-and-half between AIDS denialists and experts who maintain that HIV is the cause of AIDS.

Mary Crewe, head of the Centre for the Study of AIDS at the University of Pretoria, believes that the interest Mbeki has taken in the AIDS denialists is typical of the government's confused and paralyzed response to the epidemic. "It is as if we have just become aware of [AIDS] and are struggling to find ways to understand it," she has written.

> *"It is as if we have just become aware of [AIDS] and are struggling to find ways to understand it."*

Agonizing Inactivity

Meanwhile, potentially effective programs are languishing. In fiscal year 1999-2000, the AIDS Directorate in the Ministry of Health failed to spend 40% of its budget. The government last winter appointed a National AIDS Council, which included an athlete, a TV producer, numerous politicians and two traditional healers, but did not include South Africa's most important scientists, doctors and non-governmental AIDS organizations. Even the government's media campaigns have been criticized for being ineffective and expensive. During National Condom Week, the government distributed free condoms, which, regrettably, were stapled to a card.

Around 200 South African babies are born with HIV everyday. If they and their mothers were given AZT around the time of delivery, up to half of these babies would be spared HIV infection and AIDS. As long ago as 1997, AZT manufacturer Glaxo Wellcome offered South Africa at a 70% discount on AZT used in public maternity wards. A two-dose course of another anti-HIV drug, nevirapine, which is similarly effective at preventing mother-to-child transmission, is estimated to cost only two to eight dollars. The Health Ministry repeatedly turned down Glaxo's offer, and did not provide nevirapine, either. The government has contended at various times that the drugs were either still too expensive or too toxic. Neither will be offered to pregnant women attending public hospitals until the drugs are further investigated.

When asked what he had to offer people with AIDS, a doctor at one public hospital east of Johannesburg responded, "We have no [antiretroviral] drugs here, not even for needle-stick injuries." When doctors and nurses

accidentally stick themselves with bloody needles, they may expose themselves to HIV. Someone who is exposed to HIV through a contaminated syringe can reduce the chance of becoming infected by about 80% with an immediate course of antiretroviral drugs. Kits of such "post-exposure prophylaxis" drugs are supposed to be available in all South Africa's hospitals for health-care workers at risk of needle-stick injuries. This doctor says that they have been absent at least "since the President started talking to [the AIDS denialists]." Patricia Lambert, a lawyer who works with the Health Minister, responded that all hospitals were supposed to have antiretroviral kits for needle-stick injuries.

According to Interpol, South Africa has the highest rate of reported rape in the world. A woman's chances of being raped in South Africa are four times greater than in the United States. Charlene Smith, a Johannesburg journalist, is campaigning for the state to provide post-exposure prophylaxis in public hospitals for rape survivors. Smith herself was raped in April 1999, and a week later, she wrote a newspaper account of her race to obtain antiretroviral drugs during the hours following her ordeal. As with needle-stick injuries, these drugs can also reduce the chances of HIV infection after rape.

Aware of the need to obtain the drugs quickly, she pleaded with a series of indifferent health care workers at hospitals and pharmacies in order to obtain them. She then found that a full course of treatment, consisting of a month of AZT, 3TC and Crixivan, would cost R4500 (about $780). Had the government accepted Glaxo's offer of AZT at the reduced price, a combination of AZT and 3TC, which works almost as well, would have cost the public sector only R200 (about $33).

"We have all these plans. We plan and plan and plan...We have the fastest growing epidemic in the world, and the fastest growing number of plans to deal with it."

Smith has managed to persuade private hospitals to stock "starter kits" of three days worth of AZT and 3TC for post-rape prophylaxis, which rape survivors can purchase for R170 (about $30). But public hospitals do not stock the kits, and the full 28-day course of drugs is unavailable to most of South Africa's rape victims, who generally are poor and black.

Campaigning for Better Treatment Access

Many of South Africa's community health-care clinics are not equipped or staffed to manage persons with HIV or AIDS. Worse yet, at a recent parliamentary hearing in Cape Town, several HIV-positive individuals testified that health-care providers frequently refuse to meet their needs. Noriri Lamati said that health workers at a hospital in Eastern Cape province turned her away, even for complaints not related to AIDS. Lamati claims she was told, "You know there is nothing we can for people with HIV. They just die." Sindiswa Godwana testified that hospitals did not even dispense multivitamins for people with AIDS. The new AIDS plan may force hospitals to pay attention to people with HIV.

Antiretroviral drugs for pregnant women, rape survivors and people with HIV in general may remain out of reach, though. Dr. Costa Gazi, a Member of Parliament for the opposition Pan-African Congress of Azania who has been critical of the government's AIDS policies in the past, says that the new plan "doesn't sound very inspiring, especially because the use of antiretroviral drugs isn't included."

Zackie Achmat of the Treatment Action Campaign, an activist group that has been campaigning for affordable AIDS treatment in South Africa, says that the plan looks like a good one, and he hopes it is implemented. Still, he worries that the plan's goals are too broad. He believes that two key priorities should be the provision of antiretroviral drugs for the prevention of mother-to-child HIV transmission and access to antiretrovirals and drugs for opportunistic infections for all HIV-positive South Africans. At present, these drugs are scarce and available only at great expense from private pharmacies.

Gazi is encouraged by the fact that Health Minister Tshabalala-Msimang has endorsed efforts to press for compulsory licensing and parallel importation of patented pharmaceuticals, including antiretroviral drugs. Compulsory licensing would permit South Africa to manufacture its own generic versions of these drugs, and parallel importation would permit South Africa to import them from countries such as Thailand and India, where inexpensive generic versions of many patented drugs are already sold. "I hope she'll pursue this," says Gazi. "It's the first time we've heard this is her intention."

In 1997, South Africa attempted to enact a law that would allow parallel imports and compulsory licenses for pharmaceuticals, but a consortium of Western pharmaceutical companies tied the proposal up in the South African courts while the United States threatened trade sanctions. Glaxo Wellcome last May offered AZT and 3TC to poor countries at 20% of world market prices under certain conditions. Four other companies indicated that they might eventually offer similar discounts for their antiretrovirals. Tshabalala-Msimang again has argued that the drugs would still be too expensive for South Africa.

Achmat is encouraged that the Health Ministry may now be revisiting the push for parallel imports and compulsory licenses, but he wants to see action right away. "If the minister showed political will, it could take only about three months to get a license to import and manufacture [generic versions of patented drugs]."

Endless Planning

The real test of the new AIDS plan will in be the nature of its implementation. "The government really needs to lead on action," says Achmat. But action has not been the strong suit of South Africa's AIDS programs so far. Mary Crewe observes, "We have all these plans. We plan and plan and plan… We have the fastest growing epidemic in the world, and the fastest growing number of plans to deal with it." Crewe calls the South African response to AIDS "frozen." This paralysis, she believes, emerges from the scale of the epidemic, which is "so huge it's enough to freeze anybody," as well as from the nation's unique social complexity. South Africa is partly a modern industrialized country and partly a rural African one, so it needs an AIDS response appropriate "both to inner city New York and to rural Uganda."

For Crewe, the most frustrating thing is that the government has not drawn sufficiently on the expertise of local community-based AIDS organizations, nor has it tapped the grassroots energy generated during the anti-apartheid struggle. "I find it fascinating that Mbeki keeps talking about how the solutions have to come from the 'African people' and not from foreign experts," Crewe says, "but the South African people want AZT for pregnant women. They also want rape prophylaxis and more funding for treatment of people with AIDS. At what point do you accept what the people are asking for?"

Large Remune Trial Hits a Brick Wall

by Dave Gilden

On June 6, investigators halted enrollment in ACTG 5057, a trial of the Remune therapeutic vaccine (see the June 2000 *Treatment Insider*). The halt came barely a month after the trial began. It occurred because of a newly surfaced analysis of data from Remune trial 806, a 2,500-person trial prematurely terminated over a year ago.

Remune consists of killed HIV stripped of its outer envelope and emulsified with mineral oil. Trial 806 was stopped because the introduction of protease inhibitors and potent antiviral combinations during this trial's recruitment masked any possible benefit that Remune might have in slowing disease progression. The Immune Response Corporation, which created Remune and sponsored this trial, has widely disseminated one analysis of 250 trial participants indicating that Remune conferred modest improvements in viral load at certain timepoints.

Unpublicized viral load analyses in five other subgroups failed to find any difference between Remune and placebo. The one that stopped ACTG 5057 was a preplanned analysis by statisticians at the Harvard School of Public Health. The Harvard experts looked at "virologic failure" among 435 participants in trial 806. These people had attained viral loads below 400 before entering the trial and were taking protease inhibitor-containing combinations at entry or soon afterward.

"Virologic failure" was defined as either changing two or more antiretroviral drugs or having a viral load that was substantially higher than baseline. Half the members of this substudy experienced such failure, regardless of whether they were receiving Remune or the placebo.

One notable outstanding issue is that the number of therapy switches due to drug intolerance rather than HIV breakthrough was not recorded. Two-thirds of the treatment failures were so designated because of therapy alterations.

The subgroup's experience nevertheless casts a pall on ACTG 5057, which is specifically designed to detect Remune's effect on the time to virologic relapse. It is highly unlikely that the trial will show the benefit from Remune that its organizers anticipated: a 50% reduction in virologic relapse in the course of 96 weeks.

This 50% figure comes from Remune trial 816, a 32-week, 43-person pilot study of administering Remune or placebo to persons with relatively early HIV infection who were starting an AZT/3TC/indinavir combination regimen. Trial 816 was primarily an investigation of Remune's effect on anti-HIV immunity. The viral load breakdown was an afterthought and had questionable results. Most of the viral load difference between the Remune and placebo arms occurred during the first sixteen weeks of treatment with anti-HIV drugs, a period in which trial participants received just one shot of Remune. It is doubtful that Remune can enhance the already substantial initial effect of antiviral drugs, especially given the results of trial 806.

ACTG 5057 was supposed to enroll 472 persons. Redesigning it so that it could statistically document a smaller benefit would require a much larger and more expensive trial. Documenting a 30% difference in HIV breakthrough might require 1,200 trial participants. A 10% difference might require 12,000.

It is unclear how a large government-financed trial like ACTG 5057 was first set up based on such spurious data. Where the extra financing will come from to alter the trial is anyone's guess.

Facing the South African AIDS Challenge

by Stephen P. Laifer

A decade after the fall of apartheid, South Africa is working to resolve the political and financial aftermath of more than a half century of institutionalized inequity. Though the wounds are slow to heal, past injustices are being redressed across the board, and the country's constitution now ranks among the world's most liberal.

The biggest challenge now facing this nation of 40 million is one that collectively encompasses economic, social, political, and health issues: HIV/AIDS currently affects nearly every citizen either directly or indirectly, with 1,500 to 1,800 new cases diagnosed every day. The South African government could not have predicted that the greatest threat to its future stability would be a growing epidemic. Recent newspaper editorials by government ministers estimate the present HIV prevalence at a staggering 20% of the South African population.

And the numbers are increasing. One recent projection is that one-third of the total South African population will be HIV-positive by the year 2010. Rural communities are hardest-hit: nightmare scenarios of whole villages turned into ghost towns, overcrowded clinics with too few beds, and overwhelmed hospital staff hopelessly ill-equipped to handle the deluge of terminally ill patients, most of them under 35, are commonplace in predominantly rural provinces like KwaZulu -Natal. Burials and cremations in that province's city of Durban – site of the next International AIDS Conference in July – have risen 250% over the past three years.

The bulk of South Africa's economically active labor force hails from such rural parts of the country. "What we are seeing is nothing less than imminent full-scale economic disaster," says Dr. Ian Sanne, head of the Infectious Diseases Clinic at Johannesburg's University of the Witwatersrand. The ramifications for Africa as a whole would be devastating.

Dr. Sanne urges that industry and government work together. "They have to accept that we need antiretroviral therapy in this country, while there's still time to act effectively. The political will needs to shift cohesively to a holocaust mentality."

President Thabo Mbeki's government, on the contrary, has taken the bewildering official stance that unless AIDS treatment can be made affordable to all, it should be withheld from all. Mbeki is under fire from the AIDS community for refusing to fund badly needed AZT treatment programs for pregnant mothers, rape victims, and hospital staff accidentally exposed to the virus through needle-stick injuries. In response to such proposals, Mbeki has cited his belief that AZT is too toxic for regular use. He has also questioned whether HIV does indeed cause AIDS.

Dr. Sanne believes the South African government first needs to abandon its current unreasonable attitude before it can create any solutions. "Of course, we ideally want access to therapy for all," he says, "but we cannot wait for equitable access for everyone, before we start treating someone."

"They have to accept that we need antiretroviral therapy in this country, while there's still time to act."

Escaping the Impasse over Drug Prices

AZT, which costs a little more than half a South African rand ($0.07) per tablet to produce, sells in South Africa for R2.79 ($0.35.)per tablet. This amounts to a current monthly cost of some R500 ($71) per patient, a figure well out of reach of the average South African worker, whose salary is often less than $200 per month. Dr. Sanne is adamant that the only way to avoid full-scale economic meltdown in South Africa in the short term is to treat its economically active citizens first: "Impact studies in the mining industry alone prove its crucial that we start with the people who are the backbone of this economy. The answer lies in making drugs more affordable to these individuals. [Drugs like] AZT need to be provided to them immediately."

South African activist groups have been going head to head with the big drug companies for several years, lobbying for greater drug access for all. But Dr. Sanne feels they have possibly been approaching the problem from the wrong end. He is convinced that the only real way to ensure an improved supply of badly needed drugs in South Africa is in fact to work with the big drug companies, not against them. By appealing to their wallets and assuring them that their profits back home would remain inviolate, South Africa stands a better chance of winning them over.

Although he does advocate generic replacements, Dr. Sanne thinks it important to concentrate in tandem on reducing existing suppliers' prices. The pharmaceutical industry, he believes, is in fact shifting toward better access in the Third World. "They seem to be listening to activist groups like Médecins Sans Frontières and our local TAC [Treatment Action Campaign]. They're slowly waking up at last to the dire nature of the situation, and their attitude can definitely be changed if approached from the right angle," he says. "When and where possible, we want to take real drugs in South Africa at a lower

market price, and the current softening climate will hopefully ensure that this can happen."

Dr. Sanne is greatly encouraged by Glaxo's recently announced intention to reduce the price of AZT, 3TC and Combivir by up to 80%, but the situation is still seriously hampered by the government's attitude toward antiretrovirals in general. Since the state won't pay for antiretrovirals, it makes little practical difference how cheap the drug companies like Glaxo Wellcome may make the drugs at the consumer level.

"With the new price reduction," says Dr. Sanne, "AZT for example will now be offered to the South African government for the price of R200 per month per patient, well below the current R500 per month. If the government would only come around to agreeing on the very real benefits of AZT, then this could potentially more than triple the number of pregnant women who can currently afford AZT in the last month of pregnancy."

The Internet is actually a crucial part of the entire scheme, facilitating greater numbers of doctors involvement in AIDS.

Making the Best Use of Meager Resources

Dr. Sanne is developing a business plan that he hopes will spearhead the drive toward more affordable drugs for all South Africans. His first step concerns all-important patent rights. In the case of old patents, Dr. Sanne is pushing for South African manufacturers to be allowed to obtain the rights to produce these drugs in a much cheaper form (i.e., generics). That form should be distinct enough from the real product in terms of packaging and formulation to discourage black-market exportation to Europe, a prime source of worry for the pharmaceutical companies.

Newer drugs that do not meet the US FDA's criteria of "equivalence or superiority to existing drugs" would be targeted, too, in the hope of taking over their patents and manufacturing them locally at significantly lower expense. Dr. Sanne points out, "Just because a drug may be superceded by a newer version, that doesn't necessarily make the original drug any less effective." In both instances, patents would be held by the non-profit academic world. He contends that part of the strategy would be research. Results from continuing trials with these drugs would further benefit the pharmaceutical companies themselves.

A second step in Dr. Sanne's plan involves the development and implementation of a direct drug distribution network to patients, via the Internet. "South Africa has a highly developed, efficient network of courier systems, and these can be linked up with existing medical distribution companies via an Internet pharmacy to deliver medications door to door."

He stresses that the Internet is actually a crucial part of the entire scheme, facilitating greater numbers of doctors involvement in AIDS treatment countrywide: "Currently, there is a critical shortage of doctors willing to tackle what they see as the involved treatment of HIV-positive patients. The idea is to establish a central website for patient records. General practitioners anywhere can access these records and follow their patients' progress, and can then contact HIV specialists at the website for specific treatment advice." The model is currently in place and working in this country for diabetics, and Dr. Sanne thinks that it can be practically implemented on a much vaster scale, even in rural areas. "All it takes is one computer and a phone line in a clinic," he says.

In terms of actual treatment regimens, Dr. Sanne is part of the growing cadre of South African doctors who believe that current treatment models, based on American scenarios, may not be applicable to local conditions. "Current US criteria, such as initiating treatment when a patient's CD4 count falls below 500, need a rethink. I believe the trend here will be to rather initiate antiretroviral therapy at a later stage, say around 350, concentrating the treatment on those individuals who are already demonstrating disease progression." Besides reducing the numbers of patients who need therapy, later-stage treatment may also help address government concerns over the long-term toxicity of anti-HIV drugs.

Researching African Treatments

Dr. Sanne in addition firmly supports continued research into the long-term benefits of both nutritional support and herbal remedies in AIDS treatment. "Our proven expertise in South Africa is in the area of clinical research," he points out, "and there have been lots of developments in the phytopharmaceutical arena in particular."

Moducare, a widely used immune-system booster derived from the African potato, is only one such development, resulting from intensive local research into plant sterols and sterolins. Traditional healers in South African rural communities for generations have used the potato as a successful muti (healing compound), prompting immunologists at the University of Stellenbosch near Cape Town to take a closer look. Clinical trials identified two specific compounds, B-Sitosterol and B-Sitosterolin, which exist in all plants and are highly concentrated in the potato. These compounds do not possess antiviral

properties in and of themselves, but they demonstrate significant immunomodulatory effects and come at very low cost to the patient.

Further research is also being done on the immune-boosting and nutritional value of herbal and homeopathic remedies. Combined with widespread, cheaper antiretroviral drugs, an affordable and effective treatment regimen may indeed be possible.

Building Infrastructure with Private Funds

At the opposite end of the country, in the Western Cape Province, Dr. Ashraf Grimwood certainly agrees that more and cheaper drugs are vital, but he is convinced that the supporting infrastructure behind them is of even greater importance. “No matter how cheap the drugs are,” he states, “you need the capacity to deal with the disease first.” Dr. Grimwood, currently the principal medical officer holding the City of Cape Town's portfolio for STDs and HIV, is also the director of the scientific arm of the $100 million Secure the Future Program, a development initiative sponsored in large part by pharmaceutical giant Bristol-Myers Squibb.

Secure the Future targets South Africa and four of its neighbors – Namibia, Botswana, Swaziland, and Lesotho. The program is examining the vital links in the public health sector that come under continuous criticism. It seeks to examine those areas most needing improvement, such as the training of doctors in HIV treatment, and implement higher ethical standards and good clinical practice. Nongovernmental organizations and community service providers are also encouraged to create community-based projects pertinent to HIV/AIDS prevention and care. The most promising projects are put into place for a fixed term and studied for their effectiveness. The program financially supports them on an ongoing basis if they are found to be feasible. “It all ties in,” says Dr. Grimwood. “Capacity building and improved infrastructure on all levels lead to improved drug access for everyone.”

From a scientific standpoint, his own branch of Secure the Future examines specific research categories of HIV treatment, such as mother-to-child transmission, post-rape cases, and orphan care. Research proposals here are also supported by Secure the Future on the bases of being innovative, sustainable, and replicable. “We are interested in anything which could potentially lead to positive government policy directives,” he explains.

Like Dr. Sanne, Dr. Grimwood supports the use of AZT in the South African context, and he hopes that the Secure the Future Program could potentially play an important role in helping to change the government’s current view. “Secure the Future facilitates important research,” he points out. “The people in power should recognize that negative side effects of AZT can be managed. The research data clearly demonstrate that short-course therapies for expectant mothers have been shown to be relatively low in risk. Considering the realities of our environment, these drugs do offer good options.”

Of necessity, the program begins at the urban level, where South Africa’s infrastructure and services are most developed. The eventual aim is for it to expand outwards from there. Secure the Future cannot hope to address the government’s demands for universal treatment access. In the present early stage, it will not be able to benefit everyone, but only some. It will not, at least in the short term, alleviate the wholesale suffering and death in South Africa’s vast rural populations. But since Secure the Future is a privately funded initiative, it does not need government backing or approval to move forward.

“The idea is, you have to start somewhere,” says Dr. Grimwood, “Even in a big modern city like Cape Town, we couldn't open all our HIV clinics simultaneously. It would have been impossible. So we started them one by one. It will roll out from there.”

amfAR™
AIDS RESEARCH

Treatment Information Services

Dave Gilden
Program Director/TIS

Bob Huff
Editor-Treatment Directory

Joe Guimento
Managing Editor

Barbara Good
Treatment Information Assistant

Candida Scott Piel
Community Liason

Department of Clinical Research & Information

Kevin Robert Frost
Vice President

Jeff Smith
Project Manager

Paul Donahue
Administrative Asst

IS Department
Don Moschberger
Sue Doster
Technical & Computer Support
Larry Switzer
Glen Trejbal

Database Development / Support
Carol Harvey,
DataLan Corporation

©2000 All rights reserved.

Next Month
Reports from the 13th International Conference on AIDS, in Durban, South Africa