Therapeutics Research • Education • AIDS Training

TREAT ASIA REPORT

Change at UNAIDS: Peter Piot Moves On

Lauded for his work as a scientist, physician, and public health leader, Dr. Peter Piot stepped down as executive director of UNAIDS in December 2008. He had been at its helm since the founding of UNAIDS in 1995. Dr. Piot is credited with co-discovering the Ebola virus in 1976, and he is widely recognized for having established the foundation of our understanding of AIDS in Africa. In this interview, Dr. Piot reflects on his tenure at UNAIDS, discusses the impact of the global recession on HIV/AIDS, and considers the direction of the epidemic in Asia and around the world.

TREAT Asia Report: Many expect the global economy to get worse before it gets better. Are you concerned that this could lead to a depletion of resources for HIV programs and a reversal in some of the gains we've made in the last few years?

Dr. Peter Piot: I think we should be realistic about the potential impact of the financial and economic crisis. The incomes of the world's biggest governments are declining and expenditures are going up because of financial efforts to save the economy, which means that government budgets will face constraints. We have to be sure that this is not going to result in cutting AIDS programs. I'm not saying that's going to happen, but it's a risk that means we will have to be extremely vigilant.

The impact of the financial crisis on the spread of HIV is not clear. What we've seen in Asia, in countries like Viet Nam

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World AIDS Day

World AIDS Day gatherings across Asia included (left) a Thai Red Cross World AIDS Day parade in Bangkok, where marchers decorated their costumes with condoms, and the annual candlelight vigil in Hong Kong (center and below). (Photos courtesy Thai Red Cross and the Hong Kong AIDS Foundation.)

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The *TREAT Asia Report* is a quarterly newsletter published by amfAR on behalf of TREAT Asia–Therapeutics Research, Education, and AIDS Training in Asia.

TREAT Asia is a network of clinics, hospitals, and research institutions working with civil society to ensure the safe and effective delivery of HIV/AIDS treatments throughout Asia and the Pacific.

The information in the *TREAT Asia Report* is compiled from a variety of sources and may contain controversial views and opinions not endorsed by amfAR. Material in the *Report* should not be used as the basis for medical diagnosis or treatment.

This newsletter is also online at www.treatasia.org.

TREAT Asia Report

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A Time of Transition

This past year has been a time of great transition for TREAT Asia. After joining the Bangkok office in September, we conducted a think tank on how to better link the HIV/AIDS community to the clinical establishment in a region where the social and cultural gaps between healthcare providers and patients often are wide. This emphasis on working more closely with the community carried through to our annual Network Meeting (see story below), where we set a number of creative and challenging programmatic priorities for 2009. In order to expand our involvement with the HIV/AIDS community, we added an additional community representative (see Voices, page 3) to the TREAT Asia Steering Committee.

As TREAT Asia's programs evolve, so too will our methods of communicating about our work. As you'll notice, this issue of the *TREAT Asia Report* launches a new design coupled with a new approach to some of our content. We're particularly honored in this issue to feature an interview with Dr. Peter Piot, former UNAIDS executive director, who reflects on his years as head of the world's most influential AIDS organization. This issue also includes a new section highlighting recent research of particular interest to the HIV/AIDS community (see pages 4–5). Our goal here is to present advances in the fields of prevention, treatment, and basic science that may otherwise be difficult for patients and families to hear about or understand. Your feedback and suggestions about these changes would be most welcome.

Finally, we would like to thank our donors, investigators, and partners for their continued commitment to supporting TREAT Asia. As we enter our ninth year as an international collaboration fighting HIV/AIDS in Asia, it is clear that our strength lies in our network and the people within it.

Annette Sohn, M.D.
Director, TREAT Asia

Recent Accomplishments, Future Progress

amfAR Chairman in Attendance at 8th TREAT Asia Network Meeting

More than 150 participants from 19 countries across Asia and around the world gathered in Chiang Mai, Thailand, for the 8th annual TREAT Asia Network Meeting, 18–19 October. The meeting was bracketed by workshops specific to the adult and pediatric HIV observational databases and the TREAT Asia Studies to Evaluate Resistance.

In attendance for the first time was amfAR Chairman of the Board Kenneth Cole.

"[TREAT Asia] is a model and an extraordinary story that should be told everywhere," said Mr. Cole in his welcoming remarks. "I'm so inspired by what you all do."

TREAT Asia Director Dr. Annette Sohn also offered a warm welcome to the

Dr. Annette Sohn, director of TREAT Asia; and Dr. Arthur Chen, newly elected chair of the TREAT Asia Steering Committee.

"The Point Is That Anybody Can Get HIV"

Roberto M. Ruiz is a board member of Positive Action Foundation Philippines and project manager of a Global Fund-supported program to scale up treatment, care, and support for people living with HIV/AIDS. His work has helped secure free antiretrovirals for HIV-positive Filipinos.

I grew up in a broken family but graduated from college and was living with my mother while working at a five-star hotel in Manila. After work, I would sometimes join my friends for a night out. I was well-informed on how to prevent sexually transmitted infections and even thought about AIDS, but because of alcohol and drug use, I sometimes skipped using a condom. Some friends today make an issue out of my denial that I was gay, but the real issue was not my sexuality. The point is that anybody can get HIV.

I found out I was HIV positive in 1993 when I applied for a visa to work on a cruise ship in the US I had undergone HIV testing without any counseling and found out after a week that I was HIV positive. The first thing that came into my mind was that I could no longer work, but then I began to worry that I was going to die.

After I was diagnosed with HIV, the Research Institute for Tropical Medicines (RITM) in Manila provided me with the counseling and medical services I needed—so I realized I didn't have to die. But access to antiretroviral treatment (ART) was the most difficult issue in the early days of AIDS in the Philippines. From 1995 to 2000, there were only about 30 Filipinos in the country on ART—including me. Around half of us were covered under clinical trials; the rest paid for it out of their own pockets. The price of medication then was 30,000 to 50,000 pesos (US$800-$1,000) a month. But support for free ART ended in December 2000. So an organization I belonged to called Positive Action Foundation Philippines took the initiative, in partnership with RITM, to gain access to generic ART.

At first, it was almost impossible for us to bring the drugs into the country because of the piles of paperwork we

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Dr. Thanyawee Puthanakit of HIV-NAT and the Thai Red Cross AIDS Research Center, Bangkok (left); amfAR Chairman Kenneth Cole was given a tour of the Research Institute for Health Sciences at Chiang Mai University by Dr. Thira Sirisanthana (right).

participants before summarizing the Network's substantial progress in 2008. "Under the TREAT Asia umbrella, we have research, community, and education," said Dr. Sohn. "By far our highest priority is our research programs."

One main focus of the meeting was to explore how to strengthen TREAT Asia's links to the HIV/AIDS community and broaden the scope of activities to better serve the needs of the network and the region. Meeting participants heard presentations on a range of important topics, including substance use and harm reduction (Dr. Adeeba Kamarulzaman), adult and pediatric antiretroviral resistance (Dr. David Cooper and Dr. Thanyawee Puthanakit), and improving links between the medical establishment and the community (Dr. Patrick Li and Dr. Rossana Ditangco).

Steering Committee elections heralded a change in the Network's volunteer leadership and an increase in community involvement. Dr. Yi Ming (Arthur) Chen of Taiwan's National Yang-Ming University succeeds Dr. Adeeba as chair of the Steering Committee, and Dr. Poh Lian Lim of Tan Tock Seng Hospital in Singapore succeeds Dr. Li as co-chair. In addition, two new community representatives joined the Steering Committee: Orapin Niamnate from Thailand and Roberto Ruiz from the Philippines.

The 2009 TREAT Asia Network Meeting will take place in Bangkok, Thailand, 9–12 October. ■

When to Start?

New Study Examines Best Time to Start Treatment

A question that has plagued the HIV community for years is when to start treatment to achieve the best outcomes. In the mid-1990s, Dr. David Ho recommended "hitting early and hitting hard," meaning that antiretroviral therapy (ART) should be started as soon as HIV infection is diagnosed, and a multi-drug regimen should be used. Because treatment of HIV is life-long, however, side effects from ART can make it difficult to tolerate prolonged treatment and maintain adequate adherence to therapy.

The medications used to treat people living with HIV are effective at suppressing HIV and improving the body's natural defense system and are now being made in forms that are well tolerated. However, 12 years after the advent of highly-active ART there are still concerns about drug side effects, adherence to daily dosing, development of HIV strains that do not respond to medications, and the high costs of the drugs over the course of life-long treatment. These factors have typically led doctors to delay starting ART until a patient's immune system is weakened, as measured by lower CD4+ cell counts.

The most recent HIV treatment guidelines issued by the World Health Organization (WHO) in 2006 recommend starting ART for people without symptoms of disease when their CD4+ count is less than 200 cells/mL^3, and less than 350 cells/mL^3 in persons who have advanced HIV disease. But the 2008 US treatment guidelines recommend starting those without symptoms at a CD4+ count of less than 350 cells/mL^3. This translates to starting ART before the immune system becomes severely compromised (CD4+ less than 200 cells/mL^3) but not too early to risk fatigue from ART (greater than 350 cells/mL^3).

Results of a recent study , however, suggest that starting ART even earlier may lower the risk of death. These re-

Improving Understanding of Anal Cancer Risk Among MSM in Thailand

Among men who have sex with men (MSM), anal cancer has been diagnosed more frequently among those engaging in receptive anal intercourse and those infected with HIV. In a study conducted in the US, anal cancer was reported at an incidence of 35 in 100,000 MSM, with the risk of anal cancer among HIV-positive MSM double that of HIV-negative MSM. But in Asia, anal cancer has remained largely understudied.

Doctors can screen for anal cancer with a Pap smear, which checks for the presence of cancerous cells under a microscope, and then confirm abnormal results with a biopsy. The Thai Red Cross Anonymous Clinic (TRCAC) in Bangkok found that of the 174 anal Pap smear tests its staff performed on MSM between January 2007 and April 2008, 73 percent were normal, 13 percent were troubling but not clearly cancerous, and 14 percent had some evidence of cancer known as squamous intraepithelial lesions (SIL). HIV-positive MSM had a significantly higher rate of SIL (18 percent) than HIV-negative MSM (5 percent).

To increase regional capacity to diagnose and treat anal cancer among MSM, amfAR's MSM Initiative provided funding to TRCAC in April 2008 to establish an MSM sexual health clinic in Bangkok. The clinic provides screening and treatment for sexually transmitted infections, anal Pap smear testing, treatment of abnormal anal Pap smears, and risk reduction counseling services.

From April to September 2008, 1,719 MSM clients visited the clinic. Of these, 253 received anal Pap smears and 27 percent had abnormal results. These clients are now receiving follow-up care through the TRCAC MSM sexual health clinic. More resources are needed to study anal cancer risk among MSM in Asia and provide diagnostic screening and treatment. ■

These findings highlight the need for people to get tested earlier so they can receive greater benefit from ART.

cent findings were from a large study involving 22 research groups in North America and included data from 8,374 patients. The study examined patients with CD4+ counts of 351-500 cells/mL^3 who were being actively followed between 1996 and 2006. Their results showed a 70 percent improvement in survival for people starting ART with CD4+ counts above 350 cells/mL^3 over those patients who waited until their CD4+ counts dropped below 350 cells/mL^3.

This means that these patients from North America had a lower risk of dying when they were started on ART at a higher CD4+ count. In many parts of the world, however, people are often not diagnosed with HIV infection or started on ART until their CD4+ cells have dropped below 200 cells/mL^3. These findings highlight the need for people to get tested earlier so they can receive greater benefit from ART, and they also raise questions about whether international guidelines should be revised to encourage earlier treatment initiation. ■

Helping Children Take Antiretroviral Medicines on Time

A research study of adherence in West Africa asked the caregivers of 74 children who were receiving antiretroviral therapy (ART) whether the children had recently missed any doses of their medicines. Seventy-seven percent of the children, who were around six years old, had lost one parent or both and were being cared for by others. Fifty-seven percent of the caregivers were HIV-positive themselves and half were on ART.

Overall, 42 percent of the children had perfect adherence and did not miss a dose of ART in the four days or one month prior to the study interview, but adherence for the remaining 58 percent of children was less consistent. The researchers found that a number of factors influenced whether children took their medicines on time, including whether they were receiving certain bitter or difficult to take medicines such as protease inhibitors, they were girls, or they lived only with their immediate family and no other relatives. When caregivers found it hard to give the medication, doses were also skipped.

Researchers also asked caregivers what would help them improve the children's adherence. The adults said that financial support and guidance from healthcare providers on how to disclose HIV infection to children would be the most helpful interventions. Once children have been disclosed to, it may be easier for the caregiver to explain the importance of adherence.

This study reminds healthcare providers to offer extra adherence support for families whose children are taking bad-tasting protease inhibitors, large numbers of pills, or spoonfuls of syrup every day. Regarding the finding that girls had more problems taking their medicines on time, it was also noted that they were less likely to have a parent as a caretaker. More parents in this study attended community support groups than other caretakers. Participation in these types of groups can help families cope with social stress and share experiences with ART. Families can also help improve adherence by scheduling medicines around routine daily activities. Doctors and counselors can work with caregivers to find ways to help children take bitter medicines or swallow pills, and discuss new, easier-to-take pills when they become available. ■

Sister Tue Linh of Mai Hoa AIDS Center, Ho Chi Minh City, giving ART to a child.

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and even in China, is that economic growth and increased wealth have been associated with the spread of HIV—rather than poverty—because more disposable income generates greater opportunities for sex and drugs.

Where the impact could be the most immediate is among HIV-positive lower middle-income people or those who fall into poverty. Access to HIV treatment, care, and support could become more difficult because of increasing poverty and less access to public services.

It may be a bit early, but what's clear to me is that decisions that are being made today, in terms of how to respond to the economic crisis, will have a far-reaching impact.

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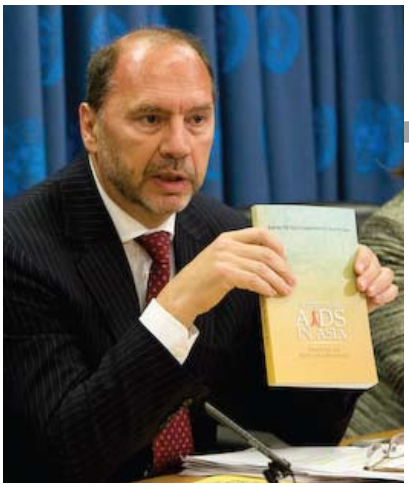

Dr. Piot was in New York in March 2008 for the release of Redefining AIDS in Asia—Crafting an Effective Response, *a report by the independent Commission on AIDS in Asia. (Photo: UNAIDS/B. Hamilton)*

TA Report: China and India account for roughly one-third of the world's population. A few years ago there was much concern that the HIV epidemics in these two countries would explode but that doesn't appear to have happened. Are you fairly confident that we've averted a catastrophe in China and India, or should we still be extremely vigilant?

Dr. Piot: First of all, there are populations in India and China with very high HIV prevalence rates—among them sex workers in some areas in Karnataka and Andhra Pradesh in India, and injecting drug users all over China and East Asia. We're also seeing new, very rapidly rising epidemics among gay men and men who have sex with men [MSM].

India's overall prevalence rate is relatively low, which gives the impression that there's no problem, but HIV doesn't have a normal distribution in the statistical sense. As I said, it's concentrated among groups such as MSM, sex workers, and injecting drug users, and there the numbers are bad.

In Asia, we need to take a long view of the epidemic. The growth of the epidemic in Asia has been slower than we anticipated, that's true, and we haven't gone into an African type of scenario in the short term. But with a denominator of one-third of the world's population, one percent in China is 13 million people and 10 million in India—more than the total population of some African countries.

One of the lessons that we've learned about AIDS is that we must expect surprises. The new epidemics among MSM all over East and Southeast Asia are a surprise but they shouldn't be. What I think is key is that the response to AIDS in both India and China has been quite good, after initial denial and hesitation. Who would have thought even five years ago that China would now have maybe 500 methadone clinics? In India, these clinics have had real, measurable results. The evolution of the AIDS epidemic is something that depends on many complex issues, one being the political context.

TA Report: You've often emphasized the link between human rights and HIV. How can we be more effective in addressing the homophobia that's such a huge barrier to preventing HIV and to establishing effective HIV interventions for MSM?

Dr. Piot: It is clear that homophobia not only constitutes discrimination against gay people and it's not only a human rights violation—it's also a major obstacle to implementing effective AIDS programs. We need to explain that over and over again, especially in societies where homosexuality is against the law. And let's not forget, that was the case in most Western countries when I was young. I come from Belgium and when I was a teenager there, homosexuality was illegal. Now we have same-sex marriage and adoption, so things can change. But they don't change spontaneously. You have to make sure that there is pressure.

Dr Piot with United Nations Secretary-General Ban Ki-Moon in New York, March 2008. (Photo: UNAIDS/B. Hamilton)

We also have to support emerging MSM groups in various countries. At UNAIDS that's something we've been doing together with amfAR. It's extremely important to push the boundaries of the system and develop a broad base of support for MSM. It can't all come from the outside, but from the outside we can support our colleagues who are fighting for their rights.

TA Report: You've been working at the Joint United Nations Programme on AIDS (UNAIDS) for 13 years and have accomplished a great deal. Is there a particular accomplishment that you're especially proud of from your tenure at UNAIDS?

Dr. Piot: I think the main achievement, if I can offer a single one, is having put AIDS at the top of political agendas and on the agenda of businesses all over the world. All the rest, in a sense, comes from there. I am also very proud that we were instrumental in reducing the price of antiretrovirals in developing countries. But I think ultimately that would not have been possible if there hadn't been political pressure and visibility.

TA Report: These days, more and more patients need to move onto second-line antiretroviral therapy, which is much more expensive than first line. What are the prospects for making those drugs affordable for large numbers of people?

Dr. Piot: With second-line drugs, we are facing the same problem we faced with first-line treatment. It's not only the price, although the price must come down. But I don't think that it's going to be that difficult this time because the toughest battles are always the first ones. Industry has seen that the markets have not collapsed and that they can still make good profits with differential prices.

But the big challenge, I think, is going to with be the middle-income countries and in Asia. For the least developed countries and the low-income countries, there is already some quite good differential lower pricing for second-line drugs. But for the middle-income economies, I see big challenges.

"What is key is that the response to AIDS in both India and China has been quite good, after initial denial and hesitation."

TA Report: On the research front, are you optimistic about the prospects for a vaccine or a microbicide?

Dr. Piot: I think for vaccines, we're back to the drawing board. The time is ripe now for better collaboration, for exchanging information, sharing data, samples, and so on, and really rethinking how we can develop a vaccine. With microbicides, it's a matter of doing the trials. I think the key message is not to be discouraged because there wasn't a home run in terms of all these trials. It took decades to develop some of those vaccines. We were probably a bit naïve and overoptimistic about what we could achieve in the short term.

TA Report: Now you're moving onto a new challenge in London to build an institute for global health at Imperial College. What will you be able to achieve there that perhaps you weren't able to do at UNAIDS?

Dr. Piot: My intention is to apply lessons from AIDS work to other fields, not only infectious diseases but also non-communicable diseases such as diabetes and cardiovascular diseases, which are taking on epidemic dimensions. It will be good to be back in academia to do research. And I'm very keen on transmitting my knowledge and on training a corps of new leaders, young people who are engaged in global health. ■

"ANYBODY CAN GET HIV"

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had to complete just to get them released from customs. So we lobbied different institutions, emphasizing our right to treatment access. We also formed a support group called the Treatment Action Group of the Philippines (TAGOP), and lobbied the Department of Health until they agreed to continue providing free ART to all Filipinos living with HIV/AIDS.

For me, the path to becoming an AIDS advocate began back in 1993 when I first disclosed my status. The day I was diagnosed I told my family and close friends. After a week, I disclosed my status to my immediate superior at work. By 2003, I had decided to open up about my HIV status on national television—to use my real identity to give a face to HIV, to represent Filipinos living with HIV/AIDS. My family agreed it was a good idea, but the reaction in my community was mixed. To those townspeople who worried I might be contagious, my family provided accurate information so they could understand. If they still had a problem after that, it was their problem.

Here in the Philippines, I have a lot of challenges now, including advocating to maintain free ART, and charting which actions TAGOP will take next. But my proudest achievement has been in setting an example to all that there is nothing wrong with being HIV positive. We are just like anybody else. ■

A First Step Toward a Cure for AIDS?

Novel Procedure Appears to Have Eliminated HIV

Dr. Jeffrey Laurence, Ph.D.

Can a stem cell transplant cure AIDS? Physicians and HIV/AIDS researchers are eager to explore this question after a brief report in February 2008 of a formerly HIV-positive patient who now shows no detectable signs of the virus after undergoing the procedure.

This case offers hope for the future, but it must be approached with extreme care and rigor. Scientists must first determine whether the stem cell transplant approach can be replicated; if it can, they must then examine which biological mechanisms are responsible for the eradication of the virus. This work might then pave the way for a more widely accessible cure.

The report, from a group of physicians from Germany, described a 40-year-old man whose HIV had been under good control for several years on antiretroviral therapy. Then he developed acute leukemia. In an attempt to cure the leukemia, he underwent a course of radiation therapy and chemotherapy in preparation for a stem cell transplant. But in his case, rather than simply using the best match among available stem cell donors, his physicians did something very clever. They also screened potential donors for a natural mutation known as delta32 CCR5. CCR5 is the primary means by which most types of HIV infect cells. People lacking this CCR5 receptor—a very small number—are resistant to infection by the most common forms of HIV.

This case offers hope for the future, but it must be approached with extreme care and rigor.

The patient's stem cell transplant was a success, although relapse of his leukemia required a second transplant using the same donor. Now off all antiretroviral drugs for almost two years, the patient continues to show no detectable signs of HIV in his blood, bone marrow, lymph nodes, intestines, or brain. To the limits of our ability to detect HIV, it appears that the patient represents a functional cure: he is off antiretrovirals, has a normal CD4 count, and exhibits no evidence of virus by ultrasensitive viral load testing.

It is possible that the patient may have been cured of HIV/AIDS. His doctors continue to monitor him closely and new tests are being conducted. But stem cell transplants are not a practical cure for HIV in any event—their cost can run up to US$250,000, they are associated with a relatively high death rate from infectious and immunologic complications, and the number of delta32-CCR5 donors of appropriate tissue type would be very small. But further research may yield key answers about this intriguing development. ■

Dr. Laurence is amfAR's senior scientific consultant.
The full story can be found at www.amfar.org.