Turning the Tide Against AIDS in India

The TREAT Asia Report Interview: Richard Gere

TREAT Asia Report: What inspired you to get involved with the struggle against HIV/AIDS in India?

Richard Gere: At the time I got involved with AIDS in India, the disease had so much stigma attached to it that I don’t think anyone knew how to approach it. Outside of the nongovernmental organizations [NGOs], many members of Indian society were essentially turning an almost blind eye to the issue. Based on the scale of devastation we were witnessing in many countries in Africa compounded by the sheer numbers and potential threat in high-prevalence areas in India, it seemed obvious that if we mobilized the communities that had influence, we’d be able to make a difference.

TA Report: Based on your long experience and connection with both India and the AIDS epidemic, what approaches to HIV/AIDS prevention seem to work best?

Gere: Making people less afraid of living with it and living around it, helping individuals recognize that simple prevention measures can be put in place to stem the spread of the virus. I think, ultimately, trying to educate communities that HIV/AIDS affects everyone, not only those infected with the virus.

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World AIDS Day

World AIDS Day 2009 marked the end of a decade that has produced significant gains against the epidemic across Asia. Events in the region included (clockwise from top): student visits to the Batu Arang Shelter Home for people living with HIV/AIDS in Malaysia; an information fair about HIV/AIDS at Bangkok’s Srinagarind Hospital; and outreach such as a World AIDS Day screen saver in Malaysia. (Photos: Malaysian AIDS Council, Srinagarind Hospital)
Hepatitis C Treatment: Optional or Essential?

Among people in Asia who acquired HIV through injection drug use, reports indicate that between 50 and more than 90 percent are co-infected with hepatitis C. Given that injection drug use is a major driver of the HIV epidemic in Asia, the lack of hepatitis treatment access for patients is a growing medical problem.

The primary challenge for clinicians and patients dealing with hepatitis in low- and middle-income countries is the high cost of medicines. Current regional prices for a 48-week combination regimen of pegylated interferon and ribavirin—the standard treatment for hepatitis C—range from about US$7,000 in Taiwan to US$12,000 in India, costs that do not include laboratory monitoring.

In December 2009, the World Health Organization met to develop a strategic plan on harm reduction for drug users in Asia and the Pacific. Pointing to the model of successful global advocacy that made antiretroviral therapy feasible, advocates, experts, and government officials proposed a goal of universal access to both HIV and hepatitis C treatments.

Researchers have clearly demonstrated high rates of treatment success for hepatitis C in Asian patients (see story on page 4). But until the prices of anti-hepatitis C medicines come down, this success will only be possible for some Asians with HIV.

As people with HIV age, they are increasingly confronting chronic illnesses such as heart disease and cancers—often at higher rates than people without HIV. In this issue of the TREAT Asia Report, we begin a year-long series on HIV and cancer—an urgent and under-researched arena that TREAT Asia is actively addressing.

This series will describe the scientific challenges faced by an innovative range of cancer research efforts facilitated by TREAT Asia and made possible through the US National Institutes of Health and its International Epidemiologic Databases to Evaluate AIDS. As the stories illustrate, the HIV care and treatment landscape is becoming increasingly complex and will require that we look beyond antiretroviral therapy alone to provide comprehensive care to people living with HIV.

Annette Sohn, M.D.
Director, TREAT Asia

Is It HIV?

TREAT Asia Partners on HIV Handbook for Clinicians

In an effort to help healthcare providers in the Asia-Pacific region facilitate earlier detection of HIV infection, TREAT Asia and the Australasian Society for HIV Medicine (ASHM) have partnered on a newly published clinical handbook entitled Is It HIV? Aimed at general practitioners working in primary care settings, the regionally focused text was created with contributions from members of the TREAT Asia Network, ASHM, and other clinical and laboratory experts.

Copies of Is It HIV? can be obtained through the ASHM website, www.ashm.org, or downloaded directly from www.treatasia.org.
More than 150,000 children are living with HIV in the Asia-Pacific region, and almost all have had the virus since infancy. With access to antiretroviral therapy (ART) and social support, these children can lead healthy and productive lives. But the infrastructure developed to care for them was created for young children—and for a growing population of HIV-positive adolescents, it is proving to be increasingly inadequate.

Members of TREAT Asia’s pediatric network—which includes clinical sites in Cambodia, India, Indonesia, Malaysia, Thailand, and Viet Nam—are experiencing this generational change firsthand. One-third of the children represented in the TREAT Asia Pediatric HIV Observational Database are now older than 12 years.

Recognizing the rapidly changing nature of pediatric HIV in Asia, in January TREAT Asia held its first adolescent HIV working group meeting, inviting researchers and orphan support experts to strategize about developing a regional adolescent research program. “More of the children under care in our network are becoming teenagers,” noted Dr. Thanyawee Puthanakit of Chulalongkorn University and HIV-NAT, Thailand. “It is time for us to grow up with our children and take the next step by focusing on adolescents. I strongly believe that our network can become a leader in this area.”

The meeting was the network’s first opportunity to identify and prioritize research questions that will help clinicians and families better anticipate the psychosocial and medical needs of adolescents with HIV. Major research interests include behavioral risks (e.g., drug use, sex), sexual health, metabolic complications of long-term ART, HIV drug resistance, and salvage therapy. “I think it is very important for TREAT Asia to begin an adolescent initiative,” said Dr. Lynne Mofenson of the National Institute for Child Health and Human Development, U.S. National Institutes of Health. “While there is ongoing research in this area in the U.S., there may be unique characteristics in Asian children that would result in different outcomes related to growth, development, and toxicity of antiretroviral drugs. Thus it is critical that the region also evaluate these issues in Asia’s youth.”

After laying out a broad research agenda, the TREAT Asia pediatric network is now moving forward with the next phase of the adolescent HIV initiative. During the coming year, investigators will develop research tools to be used in the future by the TREAT Asia Pediatric HIV Observational Database. The complexities of working with adolescents are immense and will require novel, culturally sensitive approaches. Having access to informed treatment and care calibrated to the needs of adolescents could make the path to adulthood far less challenging.

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An estimated 180 million people worldwide have chronic hepatitis C virus infection. Over time, up to 15 percent of them develop progressive liver disease, with rare cases of liver cancer. However, those co-infected with HIV have higher rates of disease progression and end-stage liver disease, or cirrhosis. In addition, co-infected patients may experience greater HIV drug toxicity and poorer responses to antiretroviral and anti-hepatitis treatments.

Treating hepatitis C can reverse cirrhosis and cure the infection. The standard medicine regimen includes pegylated interferon (given by injection under the skin once a week) and ribavirin (capsules or tablets, twice a day). This combination is taken for 24 to 48 weeks, depending on the type of hepatitis C virus in the patient’s body and on whether he or she also has HIV. Treatment leads to suppression of the virus, which can be measured by a viral load test. Patients with undetectable hepatitis C viral loads six months after finishing their medicines are said to have a “sustained virologic response” and are considered to have been successfully treated.

There are six different major genotypes of hepatitis C virus; the most common in Asia is genotype 1, which requires a full 48 weeks of treatment. In studies of HIV-negative patients with genotype 1 in China, Japan, Korea, and Taiwan, between 44 and 79 percent responded successfully to combination therapy—often higher than rates seen in non-Asian patients in Western countries. Greater expansion of hepatitis C treatment research in South and Southeast Asia would be needed to assess treatment outcomes in resource-limited settings and among HIV-positive patients.

In November 2009, the World Health Organization (WHO) released revised recommendations indicating that the antiretroviral drug tenofovir may be included in first-line HIV treatment regimens for adults, and that stavudine (known as d4T) should be phased out of global HIV programs in the future. Tenofovir costs more than stavudine, but patients only have to take tenofovir once a day. In a recently published study, researchers analyzed the cost-effectiveness of using tenofovir in first-line regimens in India to assess the feasibility of implementing this recommendation.

Cost-effectiveness research looks at the financial costs required to deliver an intervention in order to achieve a desired benefit, often described in terms of the years of life saved. Costs are compared between different interventions to find out which bring the greatest benefit for the money. Cost-effectiveness analyses can help inform national programs considering whether to implement an intervention. In this study, researchers analyzed the costs of using tenofovir (estimated in India at US$14/month) and the impact of antiretroviral therapy, drug side effects, and opportunistic infections on years of life saved.

Including tenofovir in first-line regimens in India was found to be more cost-effective than regimens with zidovudine and/or stavudine, meaning that using tenofovir resulted in more years of life saved for the costs of buying the drug and managing side effects. Having a low or high CD4 count at the beginning of treatment did not have an important effect on the results. And as the predicted price of future second-line regimens went down, the cost-effectiveness of tenofovir increased. However, if the price of tenofovir rose above US$40/month, it would no longer be cost-effective in India by WHO standards.

Although this study supports the
Protecting Infants From HIV
New WHO Recommendations for Pregnant Women

HIV/AIDS is the leading cause of death worldwide among women of reproductive age. The proportion of HIV-positive women who received antiretroviral therapy (ART) or prophylaxis to prevent HIV transmission to their infants rose from 33 percent in 2007 to 45 percent in 2008.

Despite this improvement, around 430,000 children were born with HIV in 2008, and the number of women living with HIV is steadily increasing. In Asia, women now represent 35 percent of all people living with HIV.

The World Health Organization (WHO) recently released new recommendations on the use of antiretrovirals to prevent mother-to-child transmission. The primary goals of the revised approach are to improve maternal health and reduce the risk of mother-to-child transmission to five percent or less. WHO now calls for all patients, including HIV-positive pregnant women, to begin ART when their CD4 counts fall below 350 cells/mm$^3$, or at WHO clinical stages 3 or 4. Starting ART at higher CD4 counts can prevent severe damage to the immune system, reducing the risk of HIV-related health problems and death.

For women who do not need to start ART yet for their own health, WHO has recommended that antiretroviral prophylaxis be started as early as the fourteenth week of pregnancy and continued through the breastfeeding period. This is more aggressive than WHO’s 2006 recommendation of treatment at a CD4 count below 200 cells/mm$^3$ and prophylaxis after the twenty-eighth week of pregnancy. It is also the first time WHO has promoted ART for HIV-positive mothers while breastfeeding.

However, implementing these recommendations will present feasibility and cost challenges in order to identify patients at higher CD4 counts and provide them with access to a broader range of antiretroviral options. In addition, while the global average for coverage of maternal antiretrovirals for preventing mother-to-child transmission in low- and middle-income countries is now 45 percent, in Asia it is still only 25 percent.

For specific recommendations on antiretroviral regimens for women and infants, please see http://www.who.int/hiv/pub/mtct/advice/en/.


Thai MSM Clinic Conducts Innovative Studies of Anal Cancer and HIV

Among HIV-positive men who have sex with men (MSM), the risk of anal cancer associated with human papillomavirus (HPV) is twice the level of those who are HIV negative, according to research conducted in the US. Unlike many cancers, anal cancer is potentially preventable, but many MSM are unaware of their risk of acquiring HPV and do not know to seek Pap smear screening.

In Asia, where very little research has been done on this issue, anal cancer among HIV-positive MSM has been largely overlooked and untreated. That has now begun to change, thanks to an ongoing study conducted by the Thai Red Cross AIDS Research Center in Bangkok.

In 2008, this TREAT Asia Network site established an anonymous MSM sexual health clinic providing screening and treatment for sexually transmitted infections, anal Pap smear testing, treatment of abnormal anal Pap smears, and risk reduction counseling. Funding from amfAR’s MSM Initiative allowed investigators to offer the Pap smears free of charge and facilitated the purchase of a high-resolution anoscope, which allowed researchers to better evaluate patients with abnormal Pap smears.

Analyzing the results of their early testing, researchers found that a high percentage of MSM had abnormal results—and at a much younger age than in the US (30 years and under, compared to 40-45 years in the US). In addition, HIV-positive MSM showed significantly higher rates of pre-cancerous lesions (dysplasia) than those without HIV (18 percent versus five percent).

These findings led investigators, under the guidance of Nittaya Phanuphak, M.D., to propose additional research to better characterize the problem of anal dysplasia and HPV infection among MSM. “Recognizing this as an emerging issue for HIV-positive MSM in Asia,” said TREAT Asia director Annette Sohn, M.D., “we were able to help obtain funding for the next phase of their research through the US National Institutes of Health’s IeDEA program” (see sidebar).

The first round of this new support sponsored a study of the clinical epidemiology of anal cancers among MSM. The second phase, which began in December 2009, involves basic biomedical research looking at biomarkers to provide scientific clues about how to better identify MSM with pre-cancerous anal lesions and why some men are developing persistent infection with HPV and disease progression. “We are hoping to see some interesting preliminary results from this stage of the project, which could lead to its further expansion,” Dr. Nittaya indicated.

“This is an innovative study for the region, and clearly necessary in light of Asia’s MSM-driven epidemic,” said Dr. Sohn. “These researchers are taking the science to a higher level that will teach us how to manage patients more comprehensively.”

Brochures about sexual health for MSM. (Photo: Thai Red Cross).

TREAT Asia Cancer Research

Limited data currently exist on cancer among HIV-positive patients in Asia. To improve their care and survival, researchers need a better understanding of the impact of antiretroviral therapy on cancer and the relationship between cancer and long-term immunosuppression.

Beginning in 2008, TREAT Asia launched a series of cancer studies funded by the US National Institutes of Health through the International Epidemiologic Databases to Evaluate AIDS (IeDEA), for which TREAT Asia serves as the Asia-Pacific representative. Components of this research plan include:

- Retrospective and prospective studies of cancer diagnoses in the TREAT Asia HIV Observational Database;
- Linkages between national cancer and HIV registries in Taiwan;
- Anal cancer screening and treatment among men who have sex with men (MSM) in Thailand (see adjacent story);
- Think tank on pediatric cancers in HIV-positive children; and
- Symposium on cancer and HIV in Asia and the Pacific.

www.treatasia.org
The expansion of HIV/AIDS treatment throughout Asia and the Pacific has brought hope to millions in the region who are living with the virus, but it has also created a host of complex challenges for HIV clinicians and researchers as they work to stay abreast of the latest developments in the field. Like the AIDS epidemic itself, resources and expertise vary widely from one country to the next, and the training needs of one clinical site may be very different from those of another. To address this diversity while boosting the overall quality of care in the region, TREAT Asia has created an innovative new education program that provides training specifically tailored to each setting.

“This is not a one-size-fits-all program,” said TREAT Asia program coordinator Oratai Butterworth. “It was designed to respond to the training needs of the individual sites, based on what they told us they needed in order to build their research capacity.”

Launched in late 2008 with support from the Australian government agency AusAID, the program began providing support and training in 2009 in Cambodia, China, Indonesia, the Philippines, and Viet Nam, with plans to add Papua New Guinea this year.

Researchers in Indonesia asked for training in good clinical research practice, and wanted specific information about how these standards would fit with their country’s research ethics regulations. At a training in October in Jakarta, more than 50 physicians, researchers, clinical coordinators, and data managers learned how to apply international clinical research standards to the development of study proposals, and heard a presentation on research ethics and national regulations by the secretary of the ethics committee of the University of Indonesia.

“Stigma and discrimination, a lack of antiretroviral medications and treatments for opportunistic infections, and advanced disease progression make it difficult for us to conduct research among these patients,” explained TREAT Asia Network member Dr. Tuti Parwati Merati, a principal investigator at Udayana University’s Sanglah Hospital in Bali. “This training workshop has helped me and my colleagues learn more about the disease, the ethics of conducting research, and how to communicate best with our patients.”

In Viet Nam, pediatric HIV/AIDS specialists and administrators wanted to learn how to develop research proposals to address questions affecting children with HIV in their country. In response, TREAT Asia developed a two-part training in clinical epidemiology. At the first session, held in Ho Chi Minh City in November 2009, 16 participants identified research questions they wanted to use as the basis for research protocols, which were developed through peer-review discussions in February.

Principal investigators and junior researchers in China are hoping to disseminate their research results to the broader HIV community by publishing in English-language medical journals. To help them improve their proficiency in English scientific writing, TREAT Asia organized two workshops, the first of which was held in January 2010 and was attended by 24 participants from 13 clinical and hospital settings across China. “We were extremely pleased with the enthusiasm and motivation of the participants, who exceeded workshop goals by going beyond writing scientific abstracts and beginning to prepare manuscripts,” said TREAT Asia’s director of research, Liesl Messerschmidt.

TREAT Asia’s new education and training program is also supporting longer-term projects, including laboratory capacity development in Phnom Penh, Cambodia, at the National Center for HIV/AIDS, Dermatology, and STDs, and technical support in biostatistics in the Philippines for the Research Institute of Tropical Medicine in Manila. ■
2009 Treat ASIA Research Publications


Gere: I feel that while there is still a great deal of work to be done, stigma and discrimination associated with the disease have tapered significantly. I think the government has adopted a positive attitude toward the issue, and education and treatment are far more accessible than say, ten years ago.

Gere: I think Heroes was most successful with its public service campaign. The project, launched in partnership with the Gates Foundation and Parmeshwar Godrej, energized NGOs and governmental agencies, brought the most at-risk groups into the mainstream through large public events, and directly engaged the Bollywood community to help humanize the pandemic.

TA Report: Data released by UNAIDS indicates that the AIDS epidemic in India is concentrated among vulnerable groups such as sex workers, men who have sex with men, and injection drug users. What implications does this have for fighting HIV/AIDS in India?

Gere: It means we have to work harder to reach those at higher risk and that we have to target our education efforts to reach those who are most directly threatened by HIV. Just because an infected demographic may be out of sight doesn’t mean they’re out of reach or any less important to reach.

TA Report: How have attitudes toward HIV/AIDS changed in India in recent years?

Gere: I feel that while there is still a great deal of work to be done, stigma and discrimination associated with the disease have tapered significantly. I think the government has adopted a positive attitude toward the issue, and education and treatment are far more accessible than say, ten years ago.

Richard Gere is recognized internationally for his award-winning work as a film actor and social activist. For more than 25 years, he has been deeply involved in global humanitarian issues, and is especially concerned about the spread of AIDS in India and the lack of care facilities there for people living with HIV/AIDS. He has been honored for his humanitarian work by amfAR, Amnesty International, the Elizabeth Glaser Pediatric AIDS Foundation, and the Harvard AIDS Institute. He is also the recipient of the Eleanor Roosevelt Humanitarian Award and the Marian Anderson Award.