The Global Fund, Remodeled
The TREAT Asia Report Interview: Dr. Mark Dybul

Dr. Mark Dybul was appointed executive director of the Global Fund to Fight AIDS, Tuberculosis and Malaria in November 2012. Since its 2002 inception, the Global Fund has supported more than 1,000 programs in 151 countries and programs it supports have provided antiretroviral therapy to 4.2 million people. Dr. Dybul was a founding architect of the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR) and was appointed its head in 2006, earning him the titles U.S. Global AIDS Coordinator and Ambassador. He served there until early 2009 and, before joining the Global Fund, was co-director of the Global Health Law Program at Georgetown University.

TREAT Asia Report: Donors and country governments face a range of priorities in improving public health. Why is it important that they continue to focus on HIV/AIDS?

Dr. Mark Dybul: The reason is, we’re at a historic moment. Because of advances in science, epidemiology, investments over the last 10 years, and experience on the ground, we now have the capacity to completely control HIV, as well as tuberculosis and malaria.

It doesn’t mean eliminate. It means completely control, and in epidemiological terms it would mean converting HIV from a pandemic to low levels of an endemic. And if we could do that, a relatively inefficient

Preventing Forced Abortion and Sterilization

Administering antiretroviral therapy (ART) to pregnant women and then to their infants, and instructing mothers to avoid breastfeeding in settings where that is safe and feasible can reduce the risk of mother-to-child HIV transmission to below one percent. Effective ART can also ensure that HIV-positive parents will have long, healthy lives. However, despite these medical advances, a report by the Asia-Pacific Network of People Living with HIV (APN+) showed that some HIV-positive women are being

CONTINUED ON PAGE 2

A pediatrician in Indonesia counsels a mother about HIV care for her daughter.
Access to Hope, Motherhood, and Treatment

What can almost be called an accidental cure of an American child born with HIV sent the world buzzing, while the scientific community debated whether or not it was in fact a cure (see page 3). Even so, the case inspires us to redouble our hope for a cure and our efforts to find one in a world that sometimes seems to forget that HIV killed 1.7 million people and infected 330,000 children in 2011 (UNAIDS, 2012).

Living with HIV does not mean a person has to be defined by it. Yet reports show that HIV-positive women in the Asia-Pacific are being pressured to end their pregnancies or be sterilized after delivery. This causes a mixture of sadness, anger, and frustration that we have not come far enough in our efforts to combat HIV-related stigma and discrimination (see pages 1–2). If we agree that antiretroviral therapy turns HIV into a manageable chronic disease, women with HIV should be allowed access to motherhood.

A judicial decision in India went a long way towards ensuring that people in low- and middle-income countries can access the HIV treatment they need by upholding a patent law that allows production of generic antiretroviral drugs to continue (see page 8). Until a cure is in our hands, we cannot reduce our financial and political commitments to supporting global treatment targets.

Annette H. Sohn, M.D.
This March, news broke that a child from Mississippi, who tested HIV positive at birth, had been cured of HIV. Less than two weeks later, researchers reported that 14 individuals in France had been functionally cured of the virus. Five years ago, the first case of a cure occurred in an HIV-positive man with leukemia, known as the Berlin patient. “A decade ago, almost nobody spoke of curing HIV infection as a realistic goal, yet we find ourselves in early 2013 with not one, nor even two, but three different types of HIV cure,” said Rowena Johnston, Ph.D., amfAR vice president and director of research.

"So what does this all mean? According to Johnston, ‘Much depends on how a cure is defined.’"

So what does this all mean? According to Johnston, “Much depends on how a cure is defined.” Experts currently define two categories of HIV cure. A sterilizing cure requires the complete eradication of all HIV from a person’s body. A functional cure requires only that even after patients stop antiretroviral therapy (ART), their HIV remains in remission and does not damage their immune system enough to cause any adverse health consequences.

The French cases, known as the VISCONTI cohort, are viewed as functional cures. These patients began receiving ART within the first few weeks after they became infected, a time known as acute infection. Today they still have detectable HIV in their blood, but have been off ART for an average of seven years without any signs of disease progression. However, the researchers noted that only 10–15 percent of patients who are identified during acute infection and placed on immediate treatment can expect similarly controlled infections.

It remains less clear whether or not the Berlin patient and the Mississippi child experienced functional or sterilizing cures. Trace amounts of HIV have been sporadically detected in both patients since they went off treatment, but at such minimal levels that the tests could represent false-positive results. In addition, research done to date has not identified virus in either patient that is capable of replicating, and therefore whatever is present does not appear to be causing harm to the patients.

The Berlin patient was cured after he received a stem cell transplant from a donor with a very rare genetic resistance to HIV infection, a life-threatening and costly process that cannot be recommended on a wide scale. The Mississippi child, on the other hand, was placed on ART at 31 hours after birth, before confirmation of HIV infection, an unusual approach that is not routinely practiced in the U.S. or in other countries. After 18 months of treatment, it was stopped and has not been restarted for over a year.

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This was an unusual and unexpected outcome that further research will help to explain. Nevertheless, this case has galvanized discussion about the potential for immediate treatment of HIV-exposed infants to increase the chance of curing them in the future. “The case is a startling reminder that a cure for HIV could come in ways we never anticipated,” said amfAR CEO Kevin Robert Frost.
Antiretroviral therapy (ART) has transformed pediatric HIV from a disease with a 50 percent mortality rate before the age of two in Sub-Saharan Africa into a chronic illness that can be controlled with medicines. ART works by stopping HIV from destroying CD4 cells, a type of white blood cell that prevents and fights infection. However, while the World Health Organization (WHO) recommends that all HIV-positive children under two years of age start ART, a new study shows that too few are receiving treatment before HIV causes their CD4 levels to fall to dangerous levels.

The TREAT Asia Pediatric HIV Observational Database (TApHOD) contributed to a global study of CD4 levels of children starting ART in low-, middle-, and high-income countries around the world. The analysis included data from 35,823 children (with a median age of 5.4 years) from 24 countries. It showed that more than 50 percent of children already had severely weakened immune systems, indicated by low CD4 levels, by the time they began ART. In children, severe immunodeficiency is defined by age groups as a CD4 cell proportion of total white blood cells: <25 percent (age <12 months), <20 percent (age 12–35 months), <15 percent (age 36–59 months), and either CD4 <200 cells/mm³ or <15 percent for children older than five. The median CD4 level in the children younger than five in the study was 13 percent, and 194 cells/mm³ in children five and older.

Most often, it was children younger than one who had the lowest CD4 levels and were consequently most in need of treatment. The prevalence of children who already had severe immunodeficiency when starting ART was 22 percent in co-infected individuals had an increase of 105 cells/mm³. These increases were significantly lower than individuals with HCV co-infection and HIV infection alone (both >150 cell/mm³).
Five TREAT Asia-supported research studies are being presented at the 7th International AIDS Society Conference on HIV Pathogenesis, Treatment and Prevention, which will be held June 30–July 3, 2013, in Kuala Lumpur, Malaysia.

Rates and factors associated with major modifications to first-line combination antiretroviral therapy: Results from the Asia-Pacific region

Among 4,350 HIV-infected patients in the TREAT Asia adult HIV cohort, 961 (22 percent) changed antiretroviral treatment (ART) regimens in their first five years of therapy. Patients in low-income countries tended to change medication less frequently than those in higher-income countries. Patients with more frequent CD4 and HIV viral load tests were more likely to change. Lead investigator: Stephen Wright, Kirby Institute, Australia.

Second-line antiretroviral therapy in HIV-infected patients in Asia: Results from the TREAT Asia HIV Observational Database

Of the 448 patients included in this analysis, those with an HIV viral load >5000 copies/ml or CD4 count <200 cells/mm³ at the start of second-line ART had an increased risk of treatment failure. Lead investigator: Nguyen Van Kinh, National Hospital of Tropical Diseases, Vietnam.

Non-adherence to first-line cART in HIV infected patients in Asia – TASER-M analysis

Adherence to first-line combination ART was assessed in 1,316 patients from 11 study sites in the TREAT Asia Studies to Evaluate Resistance-Monitoring (TASER-M) cohort. Sites that assessed patient adherence more frequently also had higher levels of reported adherence. Homosexual patients and injecting drug users (IDU) were more likely to have poorer adherence to ART than non-IDU heterosexual patients, and would benefit from targeted adherence support interventions. Lead investigator: Awachana Jiamsakul, Kirby Institute, Australia.

Cardiovascular abnormalities and carotid intima-media thickness among HIV-infected adolescents receiving long-term highly active antiretroviral therapy in Thailand: A cross-sectional study with HIV-uninfected healthy controls

Ultrasound assessments of the heart and surrounding blood vessels were done in 100 HIV-infected adolescents and 50 HIV-uninfected healthy controls. Although overall CD4 levels at ART initiation have somewhat improved over time, the majority of children in poorer settings are still starting ART with severely weakened immune systems. These children need to be tested earlier so that they can receive treatment before their risk for opportunistic infections, impaired growth, and slow brain development increases.

Longitudinal study of bone mineral density and vitamin D levels among perinatally HIV-infected Thai adolescents on long-term antiretroviral therapy

A bone density test, known as a DEXA scan, was performed on 47 patients. Afterwards, they received counseling to increase sun exposure and improve dietary choices. In repeat DEXA scans 12–24 months later, those with very poor bone density went from 23 percent to 19 percent. In addition, those with vitamin D deficiency improved from 28 percent to 4 percent. Lead investigator: Supapong Tunchaweng, Siriraj Hospital, Thailand.

The full text of the abstracts may be found at http://iasociety.org/AbstractSearch.aspx.
vaccine—50 or 60 percent effective—might be sufficient to move us towards ending the epidemic. So it’s really a historic moment now that we never had before. We’ve literally come by it in the last two to three years. And we need to grab it.

If we don’t, we already have indications from places like Uganda—which has increasing incidence despite very high coverage with antiretrovirals and prevention programs—that infection rates will start to go back up. If we don’t act now, we’ll miss this opportunity and it won’t come around again.

**TA Report: Are you optimistic that we’ll seize this opportunity?**

**Dr. Dybul:** I’m always optimistic. I think one of the more encouraging things is the increase in domestic contributions to HIV/AIDS programs. As countries increase their commitment to fighting their own domestic epidemics, it encourages international contributors to increase their response.

We’re finding it’s really about getting to the ‘hot zones.’ There’s never been any such thing as a global HIV epidemic. There’s a series of micro-epidemics. And even countries that have relatively low national prevalence or incidence rates have hot zones of high incidence. And countries with high incidence and high prevalence have areas of very high incidence and very high prevalence that are driving the national averages.

Those are people who are vulnerable, marginalized, difficult to reach, often criminalized—young women in southern Africa, men who have sex with men (MSM), people who inject drugs, sex workers, prisoners. We have to take a fundamentally different approach to how we view the response to the epidemic, then engage civil society more, deal with cultural issues, expand the human family.

And it means changing our thinking of what a health system is. Health systems don’t end at clinics. Health systems dig deep into the communities. Otherwise we have no chance of finding marginalized people, educating them, and providing them with services.

**TA Report: The Global Fund has a new funding model. How will it allow for more strategic investments on HIV?**

**Dr. Dybul:** In a lot of ways. I’ll highlight a couple. We’re moving away from a one-size-fits-all approach. So all people—the government, civil society, representatives of affected communities including vulnerable and marginalized groups, and other funders, including external funders—come together to support the country to utilize Global Fund resources through a concept note that contributes to achieving the goal of completely controlling HIV while strengthening the health system and fitting into the National Health Strategy. It means getting up-to-date epidemiology that’s district-by-district, which can be done very quickly by incidence surveys. And then using those data to triangulate with the people who are at risk in areas with high transmission.

Then we have to start looking in a very sophisticated epidemiological way at where the infections are, who is at greatest risk, and identify the interventions that are most likely to have an impact, and then to align that better with national health strategies. The whole package allows for a much higher impact.

**TA Report: What can we do to encourage private industry to be more engaged?**

**Dr. Dybul:** First of all, the private sector is more involved than just financial contributions. They’re involved with core competencies and expertise that’s not reflected in their financial donations. A good example is Coca-Cola, who we work with on supply chains. (RED), a tremendous organization, has new leadership that’s really pushing the boundaries, and I think we’re going to see increased contributions there.

There are a couple of things in the private sector that I think are important. The world’s a lot different than it was 12 years ago. There are a lot of companies—either multi-branches or multilaterals or new companies from Africa, Asia, Latin America—living in an environment in which HIV is epidemic. So they’re much more likely to want to be engaged.

We’re also looking at high net worth individuals who started those companies and are more interested in contributing to their community. It’s not the old approach of multilaterals with hat in hand—it’s much more sophisticated. And we’re looking at what can be contributed that’s not purely financial.

The last thing is innovative financing, which we’re very excited about. We are working on things like health insurance—bringing in insurance companies from high-income countries to develop insurance schemes in low-income countries, which is ultimately going to be a sustainable tool for health systems.

**TA Report: How are the Global Fund and the President’s Emergency Plan for AIDS Relief (PEPFAR) coordinating their efforts more closely to achieve greater combined impact?**

**Dr. Dybul:** We’ve always been very well integrated. A third of the money in the Global Fund comes from the American people so it’s incumbent upon the Global Fund and PEPFAR to be closely integrated.

But national health strategies have evolved, governments have taken greater leadership, and countries have taken
greater leadership financially. It’s a different landscape—not an emergency response any more.

**TA Report:** In 2011, coverage of services to prevent mother-to-child transmission (PMTCT) in South and Southeast Asia was just 18 percent compared to the global average of 57 percent. Why do you think the region is faring so poorly with regard to PMTCT services?

**Dr. Dybul:** First of all, like Africa, Southeast Asia is not monolithic. Some countries in the region have had a very vibrant or robust response, others haven’t. There are a lot of different reasons for this. Some of them have to do with the landscape of the country. Some have to do with political leadership. Some have to do with the investment of the countries themselves.

The Global Fund remains very active in Southeast Asia and is fully committed to remaining engaged there, but some countries in that region have a lot of money on their own and need to be committing more of their resources if there’s going to be an effective response.

**TA Report:** As you’ve said, gay men, other MSM, and transgender individuals are at high risk of HIV worldwide. What can be done to end the discrimination that so often obstructs access to health services for this high-risk group?

**Dr. Dybul:** Again, you have to look at the world not as a world but as regions. There are particularly high rates of infection among transgenders in Central and South America, and Southeast Asia. We actually have a program that was dedicated to the military in Central America for the uniformed police services to deal with stigma and discrimination against transgenders.

We are also financing programs in Central America and Southeast Asia that allow us to address the inequality and the structural issues that make it very difficult to protect transgender people from HIV infection. So it’s a mix of political change, cultural, structural change, and financing programs that begin to address these issues.

MSM are at great risk in many places and are often a key population with high prevalence, so we’re working to ensure that data are used to develop programs that will protect them from infection and increase access to services. For both people who are transgendered and MSM, that will mean addressing stigma and discrimination. We are partnering closely with UNAIDS and others to address these fundamental, structural issues.

**TA Report:** As international development aid transitions to a model of country ownership of AIDS programs, do you think there’s a danger that this may lead some countries to abandon some of these marginalized populations?

**Dr. Dybul:** First of all, country ownership doesn’t mean government ownership. The Eurasian Harm Reduction Regional Network initiative is entirely conducted through civil society. In other places, like Central America, there are governments that want to work with these issues because they see the epidemiology.

It doesn’t mean walking away from these important issues. It actually means working together in a more fundamental way, beginning with using the data to develop strategies and plans. Ultimately, that’s the only way to do it.

A lot of these issues we’re talking about are not only in low-income countries—they are also in middle- and upper-income countries. We will never be able to fund national programs in higher-income countries, so we are working to catalyze change and push some of these envelopes based on the data.

**TA Report:** You’ve been with the Global Fund now for five months. How would you characterize your experience thus far?

**Dr. Dybul:** It’s been incredibly exciting. It’s a tremendous organization. It’s going through a significant evolution in its business model at the same time that we’ve had an evolution in science, epidemiology, and 10 years of knowledge implementation, a lot of which the Fund helped to drive.

I have no doubt that collectively—using the current scientific tools, using the epidemiology, and focusing on the most at-risk groups and highest transmission areas, geographically and by risk group—we can completely control this infection. It’s a tremendous opportunity and a historic moment.
Indian Supreme Court Ruling Preserves Access to Low-Cost Drugs

In April, the Indian Supreme Court upheld a portion of India’s patent law critical to preserving the nation’s generic drug industry when it ruled that the Swiss pharmaceutical company Novartis should not receive a patent for its leukemia drug Gleevec®. India is the world’s largest producer of generic drugs and manufactures more than 80 percent of the low-cost HIV medicines used to treat HIV-positive individuals in low- and middle-income countries. The patent lawsuit threatened that life-saving supply.

“The Supreme Court’s ruling will prevent companies from further seeking unwarranted patents on HIV and other essential medicines,” said Giten Khwairakpam, TREAT Asia’s project manager for community and policy.

Novartis’s seven-year legal battle against India’s 2005 Patents Act focused on one section of the act, Section 3(d), that prohibits frivolous patent extensions for minor changes to existing drugs that do not significantly improve their efficacy. This practice is known as “evergreening” because it extends pharmaceutical companies’ monopolies on drugs and prevents generic production. The court’s decision affirmed that Gleevec is too similar to a previous drug to warrant a new patent under Section 3(d), and rejected the company’s contention that the section violates their intellectual property rights.

Loon Gangte of the Delhi Network of Positive People (DNP+) called the decision, “A crucial victory for people living with HIV and other diseases who can continue to rely on India for access to affordable treatment,” adding, “We have been filing several oppositions to patent applications on ARV medicines on the basis of Section 3(d).”

Novartis denounced the ruling as a symptom of “India’s growing non-recognition of intellectual property rights that sustain research and development for innovative medicines.” Yet India has granted hundreds of patents since it enacted its Patents Act to comply with international trade standards. The only patents it does not grant are those considered to be cases of evergreening, as opposed to real medical innovation.

Free trade agreements (FTAs) like the Trans-Pacific Partnership (TPP) now threaten to thwart this progress towards improved access to generic drugs. The U.S. and a number of countries in Asia and the Pacific are currently negotiating the TPP. As with many FTAs, current proposals require that member nations adopt stringent intellectual property provisions similar to those in the U.S. that would delay the availability of generic medicines and decrease competition among generic drug manufacturers. However, this competition caused the price of first-generation HIV medicines to plummet from $10,000 per person per year in 2000 to as low as $60 today. The price of free trade could prove to be very high for those living in the world’s poorer countries.

U.S. Budget Sequestration and Global Health: The Human Impact

According to amfAR estimates, in 2013 more than 150,000 people who would have initiated HIV treatment will not be able to, and thousands will die of tuberculosis (TB), malaria, and other treatable and preventable diseases because of cuts in U.S. spending on global health programs such as the President’s Emergency Plan for AIDS Relief (PEPFAR) program caused by “sequestration.” This series of automatic budget cuts was triggered when the U.S. Congress was unable to agree on how to manage its national spending. If left in place, sequestration will require $1.1 trillion in additional budget cuts over the next decade.

“Cuts to our global health investments through sequestration will have negligible impact on the federal debt but will do considerable damage in communities around the world facing serious HIV epidemics,” said Chris Collins, amfAR’s vice president and director of public policy. Global health funding represents just one quarter of one percent of the U.S. national budget.

Currently, the U.S. Senate is proposing an increase in funding for international HIV programs, but the House of Representatives is proposing even deeper cuts. The final outcome will not only affect those relying on U.S.-funded programs for life-saving treatments, but also their partners, children, and communities.

For more information on the impact of sequestration on global health funding, go to www.amfar.org/The-Effect-of-Budget-Sequestration-on-Global-Health/.