

HIV/AIDS in Asia

dation's Joan Kaufman (a reproductive health specialist who now heads Harvard University's AIDS Public Policy Program), and Abt's Ted Hammett decided to try to organize syringe-exchange programs in both countries.

They soon recruited Wei Lu, director of HIV/AIDS Prevention and Control in Nanning, China, and other leading AIDS officials from both regions. But several hurdles quickly appeared. China and Vietnam have had many conflicts in the past, resulting in a touchy atmosphere, exacerbated by the fact that drug use is considered a "social evil" in both cultures. They had also hoped that the U.S. National Institutes of Health (NIH) would be the main source of support for the project, but the U.S. government forbids needle-exchange programs. In the end, the Ford Foundation agreed to pay for the needle-exchange aspect of the project and hire the peer educators. NIH awarded the group a grant that will provide nearly \$2 million over 4 years. China also did not permit syringe exchange, so Des Jarlais suggested that they use a "social marketing" scheme that allows IDUs to exchange used syringes for a voucher that they can turn in at local pharmacies to receive clean syringes.

The project began in 2002, with teams of

(supposedly) former IDUs hired at each of the project's 10 sites to serve as peer educators who distribute vouchers or even clean syringes. The researchers also established baseline HIV prevalence among IDUs in each locale: 47% in Lang Son Province and 18% in Guangxi.



Field of nightmares. Peer educators working with Doan Ngu regularly remove needles from this open-air shooting gallery.

"In the absence of intervention, 18% could go to 40% in a year," says Des Jarlais, who notes that this is the first research project attempting to stop HIV's spread across international borders.

Open borders

Walking up to a broken wall from the old schoolhouse, Ngu points out evidence of the project's impact. A dirty Styrofoam container and a wicker basket each hold mountains of used syringes that the peer educators have collected from the abandoned lot, to prevent both their reuse and accidental needle sticks. "That's just from 1 week at this site," Ngu says.

Before burning these syringes, the project workers count them: From January through December 2002 alone, they totaled 163,827 in Lang Son Province. The Vietnam arm of the project also distributed more than 25,000 new syringes in that period. Preliminary data show that the prevalence of HIV has not increased in Lang Son in more than a year, further evidence that the program has made some headway.

Ngu well recognizes the limits of the project and would much like to see Vietnam embrace a more comprehensive harm-reduction program, including offering methadone. "We need to work harder to explain things to our policymakers," says Ngu. "They're still mixing up and confusing the political with the HIV/AIDS problem. Now's the time for action. I say this not because I'm a fortune-teller. It's because we have learned from other countries." **-JON COHEN**

Two Hard-Hit Countries Offer Rare Success Stories

By heavily promoting condom use, Cambodia and Thailand have blunted their epidemics, but the virus continues to make headway in some populations

CHIANG RAI AND BANGKOK, THAILAND, AND PHNOM PENH, CAMBODIA—On a moonless evening, a group of female and transgendered sex workers wearing identification

cards around their necks strolls through a park that abuts a Buddhist temple in downtown Phnom Penh. The dark park has a wide variety of sex for hire. Men seeking men head for the fountain. Straight women sit on the grass with small piles of oranges in front of them, a thinly veiled cover for negotiating

have worked this park themselves many a night, but this evening they have a different mission: Oxfam Hong Kong has hired them to distribute condoms.

Like neighboring Thailand, Cambodia has mounted a "100% condom program" that, with help from sex workers them-

selves, aims to persuade everyone selling or paying for sex to use a condom with each encounter. Supported by government and nongovernmental organizations, the campaigns have yielded measurable successes. In Cambodia, HIV prevalence among all adults fell from 4% in 1999 to 2.6% by the end of 2002, by which point the Ministry of Health estimated that a total of 259,000 Cambodians had become infected since the first case surfaced in 1991. A recent study by the Cambodian Ministry of Health projected that without increased condom use and other behavior changes, Cambodia would have had about three times as many HIV infections.

Thailand, which recorded its first HIV case in 1984, by 1991 had already launched a nationwide 100% condom campaign. Although national figures do not exist for the early years of the epidemic, prevalence has stabilized at around 2%. "Most of the data confirm that prevalence declines after 1993, 1994," says Sombat Thanprasertsuk, who directs the Ministry of Public Health's AIDS branch. A recent model by his office similar to the Cambodian one suggests that if the country had not attempted to thwart HIV, 10% of the population would have become infected by 2000. "The condom program re-

THAILAND & CAMBODIA

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PHOTOS BY MALCOLM LINTON

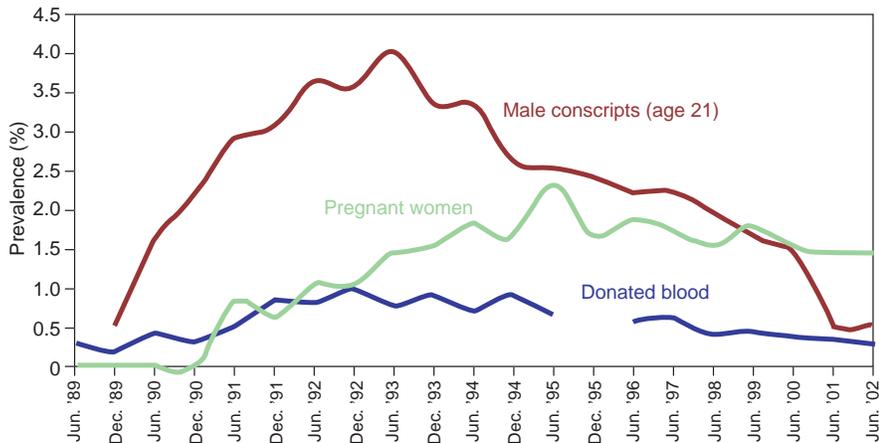


Grassroots prevention. A member of the Women's Network for Unity (in green) promotes condom use in a Phnom Penh park that has a flourishing sex trade.

HIV prevention on a national level," says Mastro. "There really had not been a demonstration that a heterosexual epidemic could be changed by behavioral interventions and condom campaigns."

Today, leading AIDS epidemiologists routinely cite Cambodia and Thailand as examples of how aggressive prevention campaigns championed by enlightened governments can dramatically slow the spread of HIV. True enough. But the accolades tend to blur the fact that these two countries have extraordinarily different AIDS epidemics. And in spite of the successes, HIV, abetted by government policies that are far from progressive, continues to gain ground in some populations.

HIV Prevalence Among Pregnant Women, Male Conscripts, and Donated Blood in Thailand, 1989–2002



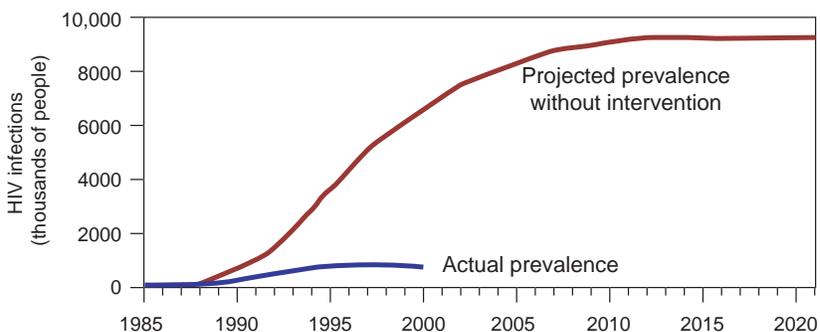
Thai troubles

At Saen Sok village in the lush mountains that surround the northern Thai city of Chiang Rai, four HIV-infected men and women from the Akha hill tribe sit at their chief's house under the shade of a sala, an open-air hut. Mingaw Huyi, who has one of her five children lying in her lap, became infected by her husband, a heroin addict who died from AIDS 3 years ago. The other three adults became infected because they shared needles themselves, and each has spent time in prison for heroin possession. One, Sompong Joebaw, 34, started injecting heroin 17 years ago, along with all of his closest friends. "I'm the only one left," he says. "They've all died from AIDS." Myat Htoo Razak, who heads a project for Family Health International that

Turning the tide. Thailand's aggressive condom campaign receives much credit for dramatic drops in prevalence in military recruits (above). A model (right) shows how stabilizing the epidemic has likely averted millions of infections.

ally worked," says Jordan Tappero, head of the large HIV/AIDS program in Thailand run by the U.S. Centers for Disease Control and Prevention (CDC). "It's very unusual that a woman in a brothel would accept a client without a condom."

Both the Thai and Cambodian programs have achieved even more impressive results among specific high-risk groups. "Consistent condom use" by Cambodia's brothel-based sex workers increased from 51.3% to 89.8% between 1998 and 2002, and HIV prevalence in that group plummeted from 42.6% to 28.8%. Another study conducted by Cambodia's national HIV/AIDS program shows that 75.8% of urban police reported having paid for sex in 1997, but that number had dropped to 32% by 2001.



In Thailand, that same population's prevalence dropped from 28.2% in 1996 to 12.27% in 2002. Timothy Mastro, Tappero's predecessor at CDC's Thailand program, says he well remembers the "tremendous excitement" when evidence first surfaced in 1995 that the prevalence in new military recruits had begun to drop in lockstep with increased condom use. "The Thai success was extremely heartening for everyone doing

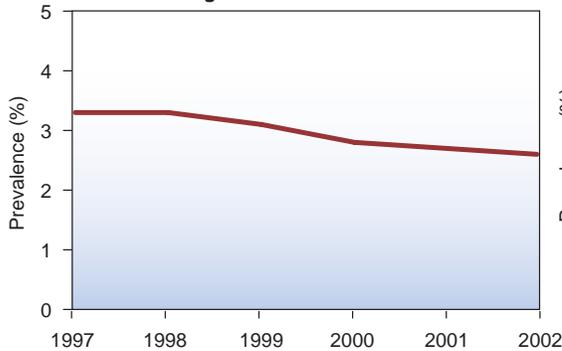
aims to lower the spread of HIV in the Akha, says that "hill tribes disproportionately have been affected by HIV/AIDS, and a lot of them have died already."

As the Akha see it, HIV continues to thrive in their community because of government discrimination. "There's an obvious prejudice against hill tribe people," says Micu Joebaw, 45, who says she began injecting more than 20 years ago and has lost one

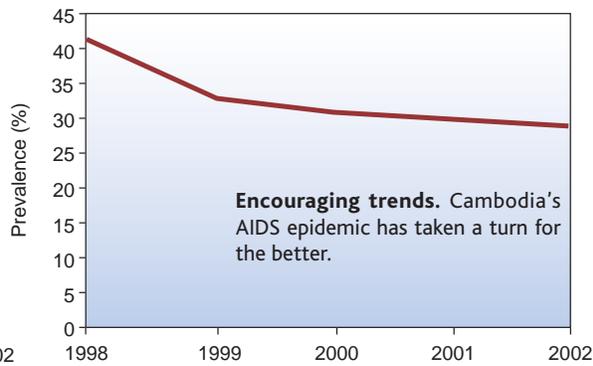
GRAPH SOURCE: THAILAND'S MINISTRY OF PUBLIC HEALTH

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National HIV Prevalence Among Adults Aged 15–49 in Cambodia



Prevalence of HIV Among Brothel-Based Sex Workers



husband to AIDS, another to a bullet, and a son to suicide. Hill tribes speak their own languages, and many people here understand little Thai, which means that the bulk of HIV/AIDS education campaigns in Thailand have no impact on them. Many Akha—some of whom are refugees from Myanmar—do not have Thai citizenship, severely limiting their access to government services. Sompong had Thai papers, but they were revoked because of his drug use. They say the discrimination pervades the services that they do receive, too. Mingaw, who learned she was infected with HIV from a routine blood test during her last pregnancy, says the Thai nurses at the hospital where she gave birth publicly chided her for being infected. “I was very angry.” Mingaw starts to cry. “But I couldn’t say anything or it would get worse.”



IDUs fight back. Activist Paison Tan-Ud advocates for drug users’ rights.

The chief, Teerawat Pitakpraisri, worries greatly about the future of his villagers. “In the past, drugs have been the number one problem,” says Teerawat. “From now on, HIV will be the number one problem for their health, the burden to their family, and the community. The young especially will have no future and, in time, they’ll get into this vicious circle.”

HIV in injecting drug users (IDUs) among the Akha and other hill tribes represents a dramatic example of a problem that extends throughout Thailand. Since researchers started routinely assessing HIV infections at drug-treatment clinics in

1989, the HIV prevalence in IDUs of all ethnicities has remained steady at about 40%. A report issued by the World Bank in November 2000, *Thailand’s Response to AIDS: Building on Success, Confronting the Future*, bluntly spelled out the situation. Written by World Bank economists Martha Ainsworth and Agnes Soucat in collaboration with epidemiologist Chris Beyrer of Johns Hopkins University’s Bloomberg School of Public Health in Baltimore, Maryland, the report noted that “the pragmatic ap-

Paison Tan-Ud, who helped organize the group. The network sharply criticizes the services that do exist. Methadone maintenance programs, it says, are restricted to Bangkok, and even those limit dosing to 45 days. “Methadone maintenance should give you methadone as long as you want it,” contends Paison. The clinics also taper doses, which he says leads many people to start using heroin again while receiving methadone. No needle-sharing programs exist, either, and regulations currently prohibit users of illegal drugs from receiving anti-HIV drugs. The World Bank report, which explored these shortcomings in de-

Can a Drug Provide Some Protection?

PHNOM PENH, CAMBODIA—Carpet-bombed by the United States during the Vietnam War, devastated by Khmer Rouge genocide that killed nearly 2 million people, and then occupied by the Vietnamese until United Nations soldiers restored order in 1993, this country has had to build a functioning public health system from the ground up. Little wonder, then, that scant biomedical research occurs here. But now, a collaboration has begun between Cambodian scientists and an international team of researchers on a cutting-edge HIV prevention study that raises eye-popping possibilities—and profound ethical dilemmas. “If this project works, it’s going to be groundbreaking,” says Kimberly Page-Shafer, an epidemiologist at the University of California, San Francisco, and one of the three principal investigators.

The study builds on intriguing monkey research, first published in *Science* 8 years ago (17 November 1995, p. 1197), indicating that the anti-HIV drug tenofovir can prevent monkeys from becoming infected with SIV, HIV’s simian cousin. Page-Shafer’s team and its Cambodian and Australian co-investigators plan to test whether a daily dose of tenofovir can similarly block HIV in uninfected people. In all, the 2-year, placebo-controlled trial hopes to enroll 860 sex workers who are at high risk of becoming infected. “It’s a prevention study that has a very high chance of providing a positive result quite quickly,” says co-principal investigator John Kaldor, an epidemiologist at the University of New South Wales in Sydney, Australia, who is working for the U.S.-based Family Health International.

The team hopes to start recruiting for the trial in January 2004. Kaldor and Page-Shafer, along with co-principal investigator Ly Penh Sun of the Cambodian National Center for HIV/AIDS, Dermatology, and STDs, have received approval from the Cambodian government and secured funding from both the U.S. National Institutes of Health and the Bill & Melinda Gates Foundation. Expectations are high: “It’s one of the few things I have heard about that might work as a preventive,” says AIDS vaccine researcher Ronald Desrosiers, head of Harvard’s New England Regional Primate Research Center in Southborough, Massachusetts.

Not surprisingly, the study—similar versions of which will take place in Cameroon, Ghana, Nigeria, and the United States—has attracted intense scrutiny. “Many people are

GRAPH SOURCE: CAMBODIA’S MINISTRY OF HEALTH; PHOTOS BY MALCOLM LINTON

tail, urged Thailand to launch “a major new effort” to prevent infection and transmission of HIV among IDUs. Otherwise, the report warned, “IDUs will continue to be a reservoir of infection and will pass HIV not only to other IDUs, but their sexual partners and children.”

Sombat of the Ministry of Public Health’s AIDS branch readily addresses the limitations to Thailand’s success story. As for the hill tribes and discrimination, “we know there’s a problem there,” says Sombat, stressing that both the government and non-governmental organizations are attempting to improve the situation. “We must do something fast, as quickly as possible.” For IDUs, Sombat says he supports harm-reduction principles, which aim to treat addiction as a disease rather than a crime. “The behavior of sharing needles and equipment among IDUs is hard to change,” says Sombat. And he acknowledges the shortcomings of their current treatment programs. “We know from the past that treatment for heroin users has a limited effect,” he says. “The percent who are cured is quite low.”

Cambodia’s conundrum

Oddly, considering the plight of Cambodia’s neighbors, injecting drug use has played no measurable role to date in the epidemic in Cambodia. No one has a con-



Hill tribe hardship. HIV-infected Akha say government discrimination fuels epidemic.

vincing explanation for this—some suggest that poverty or the strict rule of the past kept drugs out of reach—but Hor Bun Leng, deputy director of the AIDS pro-

gram run by Cambodia’s Ministry of Health, worries that the situation might change. “You can see rising drug use here with smoking and sniffing, and that later could become injecting,” he says. “And if we have IDUs, the outbreak will be more serious than ever before.”

But there is another, immediate concern: HIV continues to spread through Cambodia’s thriving sex industry, in spite of successful efforts to increase condom use. Rosanna Barbero, a coordinator for Oxfam Hong Kong, and many others note that the number of sex workers—and the spread of HIV—exploded in 1993 when the United Nations sent more than 20,000 troops to the country to help restore order.

On a lazy Saturday morning in Phnom Penh, a group of sex workers who have gathered at the old Kong Kea Restaurant, a barge parked on the banks of the Tonle Sap River that serves as headquarters for Oxfam Hong Kong, highlights the stark limitations of condom campaigns and guffaws at the notion that the government has an enlightened position toward sex work. Indeed, frustrated by their government, sex workers formed the Women’s Network for Unity 3 years ago, which has its office at the barge.

Although Cambodia, like Thailand, outlaws sex work, the government registers brothels and requires the women who work in them to visit clinics once a month for checkups to see whether they have any sexually transmitted diseases. But Barbero, who since 1999 has helped sex workers “empower” themselves, says that “ordinary people” do not like brothels. “Even men who regularly use brothels think it’s against the culture,” Barbero says.

The clash between Cambodia’s cultural mores and the thriving sex work industry came to a head on 21 November 2001, when Prime Minister Hun Sen suddenly ordered all brothels shuttered. “It was very irresponsible for the prime minister to wake up one morning and say ‘Close the brothels’ without looking at the consequences,” says Mu Soc Hua, minister for women’s and veterans’ affairs, who dressed up as a sex worker 2 days after the raids to see their effects firsthand. “The crackdown led girls onto the street, which led to more rape. And no one uses a condom during a rape, so it led to more spread of HIV. It also gave the

concerned,” says Philippe Glaziou, an epidemiologist at the Pasteur Institute here. Not only will the study give people who do not have HIV a potentially toxic drug, but it could backfire, says Glaziou. “Obviously, if you tell prostitutes they might get some protection from drugs, they’ll tend to think that they can have sex without condoms and make more money,” he cautions. “On the other hand, it’s quite interesting to know whether tenofovir would be effective.”

The tenofovir researchers have thought long and hard about these issues. They selected tenofovir because it requires only one pill a day (it has a long half-life) and has fewer side effects than any anti-HIV drug available. “It’s a very benign drug,” says Kaldor. And although the researchers have serious concerns about “behavioral disinhibition,” they will try to counter it with intensive counseling, condoms, and tests and treatments for other sexually transmitted diseases. Page-Shafer notes that preliminary data from an AIDS vaccine efficacy trial just being completed in Thailand (see p. 1663) has found that the injecting drug users who participated in the trial *reduced* their high-risk behavior.

The research that paved the way for this trial was a 1995 monkey study, in which an injectable form of tenofovir given daily completely protected monkeys intentionally given SIV. Gilead Sciences in Foster City, California, subsequently made a pill form of tenofovir for infected patients to use in combination with other anti-HIV drugs. The U.S. Food and Drug Administration approved it in October 2001.

In November 2001, researchers published another monkey study that raised a mind-bending possibility: Tenofovir might indirectly affect the animals’ immune systems and might even help them contain newly acquired infections. A research team led by virologist Jeffrey Lifson, a contractor at the U.S. National Cancer Institute, in November 2001 reported that it infected five animals with a highly lethal strain of SIV and the next day began a 28-day course of treatment with tenofovir (*Science*, 28 June 2002, p. 2325). The animals’ immune systems completely controlled the infection and then by some as-yet-undefined mechanism defeated a subsequent “challenge” with a different strain of SIV.

Desrosiers, who collaborated on the study with Lifson, says that the Cambodian study in humans—although it is intended to prevent people from becoming infected—may inadvertently shed light on Lifson’s still-confusing results. “I’m more excited about this than anything I’ve heard about in a while,” says Desrosiers.

—J.C.

Thailand's Do-It-Yourself Therapy

BANGKOK, THAILAND—Eight people dressed in matching blue protective gear, wearing face masks or complete oxygen hoods, sit together at a long table, looking for all the world like disease detectives preparing to attack an outbreak of a rare virus ravaging the local population. Indeed, that's their mission, but they're not bug detectives. These workers are in the vanguard of a movement to bring anti-HIV drugs to patients in poor countries at affordable prices: They spend their days filling bottles with anti-HIV pills (the masks prevent inhalation of the medicine) that the Thai government is manufacturing and plans soon to make widely available here.

In April 2002, the Government Pharmaceutical Organization (GPO), which employs these workers, began producing a generic version of three anti-HIV drugs—d4T, 3TC, and nevirapine—mixed together into one pill called GPO-VIR. Treatment requires only two pills a day, each of which costs a mere 50 cents. About 5000 Thais now receive GPO-VIR, but by the time Thailand hosts the XV International AIDS Conference in July 2004, the country plans to offer GPO-VIR to 60,000 of its 600,000 HIV-infected people. "This



Opening doors. GPO's Thongchai Thavichachart.

of Thailand's Ministry of Health emphasizes that far more obstacles exist than simply providing GPO-VIR. "It's lifelong care," says Taweessap, adjunct director of an HIV/AIDS collaboration with the U.S. Centers for Disease Control and Prevention. "We need a lot of training and partnerships; we need infrastructure and cooperation with nongovernmental organizations. And we're really concerned about the budget." Praphan Phanuphak, who heads the HIV Netherlands, Australia, Thailand Research Collaboration, also urges his government to start negotiating with other generic manufacturers now to buy more anti-HIV drugs to help people who fail on GPO-VIR. "It will take years for GPO to produce other drugs," says Praphan. "There are many more drugs from India that are cheap."

A Belgian branch of Médecins Sans Frontières (MSF) already has begun training Thai clinicians in the best use of GPO-VIR, but some of the most basic tools remain in short supply. Paul Cawthorne, who heads the MSF program, says it "is a nightmare" to get a person's CD4 count, a relatively expensive measurement of a key white blood cell that indicates the stage of a person's illness and is used to monitor the effectiveness of treatment.

Yet Cawthorne takes heart from Thailand's recent push with GPO-VIR and bristles when outsiders caution that the drugs in this cocktail have serious limitations. True, they have less than optimal potency, and d4T in particular can cause serious side effects. "People in the West keep saying it's not the best," says Cawthorne. "OK, d4T is not a brilliant drug. We have to accept that Thailand, even though it seems to be wealthy, it's not wealthy in its ability to afford all the drugs it needs."

Cawthorne notes that when he started working in Thailand 6 years ago, he had to fight to find a hospital bed so that someone dying from AIDS could receive the most basic medical care. "GPO-VIR is a major, major step," says Cawthorne. "The thought that as of now you would have people on triple therapy was beyond our wildest dreams."

—J.C.



Quality control. Workers hand-inspect freshly made GPO-VIR.

means a lot for Thailand," says Thongchai Thavichachart, a clinician who runs GPO. "It is the time for us to help our people."

It also means a lot to some pharmaceutical companies, which have fought to prevent the manufacture of generic versions of their patented drugs. The World Trade Organization explicitly underscored in 2001 that countries had a right to "protect public health" and "promote access to medicines for all." But Thailand and other generic manufacturers still face challenges from the pharmaceutical industry, which now focuses on some finer points of the law. "We're not going to compete with any big company," says Thongchai. "We're a small plant only for serving

police more freedom to raid brothels."

Hor Bun Leng readily acknowledges the government's murky policy toward sex workers but says that from the perspective of the Ministry of Health, the policy-makers also deserve credit for helping slow the spread of HIV in this most vulnerable group. "Part of the success story is that the government allows us to work with high-risk populations," says Hor Bun Leng. "They open the door."

Hor Bun Leng stresses that residue from the country's politics of the past confronts him more profoundly than any current political obstacles. The Khmer Rouge-led genocide in the 1970s that killed nearly 2 million Cambodians—including his parents and siblings—left a severely impoverished population, and not just financially. "Because they survived this event, they have had limited information and education," he explains. This, in turn, makes it more difficult to com-

pel them to change high-risk behaviors.

Hor Bun Leng says that in spite of the real decreases in prevalence and dramatic increases in the use of condoms, this is no time for Cambodia to drop its guard. "Cambodia looks like a patient who has recovered from a disease," he says, "but it's very easy to go back." Indeed, he adds: "We still have the highest prevalence of HIV in the world outside of Africa."

—JON COHEN

PHOTOS BY MALCOLM LINTON