

HIV/AIDS In Resource-Poor Settings: A Province in China

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AT THE DAWN OF THE THIRD MILLENNIUM, IT IS CLEAR THAT HUMANITY is facing one of the most devastating epidemics in human history—an epidemic that threatens development in major regions of the world. Since the 1960s, most countries have made impressive strides in human development. However, such achievements are being undermined as countries lose young, productive people to the epidemic. Life expectancies fall, the death tolls rise, households fall deeper into poverty, and the costs of the epidemic mount.

In some countries, the HIV/AIDS epidemic is still in its early stages and is still unfolding. This is certainly the case in China, which appears to be on the verge of catastrophe. As explained by Dr. David Ho, who has been working rigorously with colleagues in the United States and China to answer the call for an urgent and proper response, there are many villages in China where the majority of the population is infected. “Most of those infected with HIV do not have access to even the most basic services for care or support,” he said during his introductory remarks at the December 2002 PRN meeting. “As for those who are not already infected with the virus, many lack basic knowledge and information that can protect them from infection.”

Dr. Ho and his colleagues believe that it's still possible to prevent the worst from happening. A prime-boost vaccine, designed with China in mind, is currently finishing up preclinical testing and slated to enter clinical trials in China's Yunnan province—one of the hardest hit and most susceptible areas in the country.

China Basics

CHINA'S POPULATION, THE LARGEST OF ANY NATION, CURRENTLY STANDS AT 1.3 billion. In terms of geographic area, China is spread out over 3.7 million square miles—slightly smaller than the United States—with a 4,000-mile coastline that fronts on the Yellow Sea, the East China Sea, and the South China Sea (see Figure 1). It shares borders with 14 countries: in the east, with Russia and North Korea; in the north, with Russia and Mongolia; in the west, with Tajikistan, Kyrgyzstan, Kazakhstan, Pakistan, and Afghanistan; and in the south, with India, Nepal, Bhutan, Myanmar, Laos, and Vietnam.

China comprises 22 provinces: Anhui, Fujian, Guangdong, Guizhou, Hainan, Hebei, Henan, Hubei, Hunan, Gansu, Jiangxi, Jiangsu, Qinghai, Shaanxi, Shandong, Shanxi, Sichuan, Yunnan, Zhejiang; and in the northeast (Manchuria), Heilongjiang, Jilin, and Liaoning. There are also five autonomous regions: Tibet, the Inner Mongolian Autonomous Region, the Ningxia Hui Autonomous Region, the Guangxi Zhuang Autonomous Region, and the Xinjiang Uygur Autonomous Region. The country also has four government-controlled municipalities: Beijing, Chongqing, Shanghai, and Tianjin. China officially divides itself into 23 provinces, numbering Taiwan as its 23rd. Hong Kong became a special administrative region of China in 1997, and Macao achieved this status in 1999.

On the Verge

THE EPIDEMIOLOGY OF HIV AND AIDS IN CHINA REMAINS SOMETHING OF a mystery. At the end of 2001, the number of cumulative confirmed HIV infections reported by the Chinese Ministry of Health (MOH) was 30,736, with 1,594 AIDS cases, and 684 deaths related to AIDS (UN Theme Group, 2002). But Dr. Ho and others—including authorities at UNAIDS—suggest that these numbers are much lower than the reality. Most reported cases in China involve people who have been hospitalized or incarcerated, and thereby tested within these institutions. Dr. Ho reckons that there is a huge number of underreported cases, especially in rural areas, because of the lack of testing equipment, the lack of trained health officials, and the lack of voluntary testing and counseling services.

The estimated number of HIV/AIDS cases in China tells a different and probably more realistic story. The MOH national HIV/AIDS sentinel surveillance system has been in operation since 1995 and remains the principal source of information concerning HIV prevalence over time, in population groups of specific interest. The collection of data is done twice a year on five population groups: patients with sexually transmitted diseases, prostitutes, drug users, truck drivers, and pregnant women. Tests are performed at more than 100 sentinel sites within all of China's provinces, with more than 50,000 tests being conducted annually.

The MOH estimated that there were 600,000 people living with HIV infection at the end of 2001. By April 2002, the MOH updated these figures and suggested that there were between 800,000 and 1,500,000 people living with HIV infection in China. This translates into an adult HIV prevalence rate of less than 0.2%. Perhaps the most disturbing estimate was provided by the MOH in 1998—a stipulation that, by 2010, a total of 10 million people will likely be infected with HIV if countermeasures are not taken (UN Theme Group, 2002). “But many of us believe that current and predicted estimates are actually much, much higher,” Dr. Ho said.

The IDU Problem

WHILE HIV INFECTIONS THROUGH ALL TRANSMISSION ROUTES ARE INCREASING in absolute numbers, approximately 67% of new HIV infections are related to the sharing of needles among injection drug users. Unfortunately, intravenous drug use appears to be on the rise in China. A report from the National Narcotics Control Commission showed that, in 2000, the police identified more than 96,000 drug users, which is up by 49% from 1999 (UN Theme Group, 2002).

Geographically, the worst affected areas are in southern China, which is near the Golden Triangle. The Golden Triangle, which comprises 38 million hectares of rainforest-covered mountains in Laos, Thailand, and Myanmar, is a significant producer and exporter of heroin, opium, and crystal methamphetamine, much of which is trafficked through China to reach Central Asia. The drugs most likely enter China through the Yunnan province, travel through the central provinces of Sichuan and Qinghai, and eventually exit the country through the Xin-



jiang Uygur Autonomous Region in the northwest (Tibet's rugged terrain had rendered it a road less traveled by drug traffickers). As a result of the trafficking of drugs through China, provinces in and surrounding its path have experienced a proliferation of resident intravenous-drug using populations.

Numbers, of course, speak louder than words. In 2000, the HIV infection rate among IDUs were greater than 80% in Ruili, 75% in Wenshan, 58% in Kaiyuan, and 70% in Yingjiang, four cities in the Yunnan province. And in the Xinjiang Uygur Autonomous Region, rates of HIV infection among IDUs were 84% in the city of Yining and 29% in the city of Urumqi. In the Guangdong and Jiangxi provinces, as well as the Guangxi Zhuang Autonomous Region, infection rates are between 12% and 40% in various cities and appear to be worsening (MOH, 2001; Guangxi Epidemic Station, 2001).

Illegal Sales of Blood Plasma

IN A NUMBER OF PROVINCES—MOSTLY NOTABLY HENAN, ANHUI, SHANXI, and Shaanxi—in Central China, a somewhat different epidemic has been brewing. This one involves the collection of blood plasma by unregulated blood-processing companies. It is well known that many poor rural farmers have been selling blood and plasma to these commercial companies to supplement their income. It is also well known that many villagers, possibly hundreds of thousands, have been infected with HIV in the process.

These blood-collecting companies have mostly operated illegally and collected profits by selling blood products domestically and internationally since the early 1990s. With the padlocking of official Government blood-collection centers in 1995 to 1996—the hygiene practices at these sites were in no way immaculate—blood-collection companies turned their attention to clandestine blood-collection centers that

sprouted up in remote, impoverished areas in order to circumvent interference from government authorities.

“These blood-collection sites have been a nightmare in terms of the spread of blood-borne pathogens,” Dr. Ho commented. As a part of their blood-collection practices, blood from numerous donors is collected and mixed. The pooled plasma is separated from the red blood cells and the red blood cells are then reinfused back into donors. “There’s this belief, particularly among the Chinese, that blood cells are precious and that they should be reinfused if they are not needed,” Dr. Ho said. As for the medical logic behind this practice, reinfusing blood cells reduces the risk of anemia occurring, which ultimately allows donors to continue feeling well after making a donation and, thus, to sell plasma much more frequently.

These illegal blood-collection centers were at their peak soon after the closure of the government collection centers. While there has been

a decline in paid plasma donations in recent years, the practice is still very much alive and well. “We believe that numerous people were infected in 1995 and 1996, when the number of underground blood-collection centers was at its peak,” Dr. Ho said. “If you think about the typical course of HIV progression, it’s highly likely that we’re soon going to see the full impact of this epidemic. It is now believed that there may be one to three million infections within this region, which would lend to significantly higher estimates put forth by the Chinese authorities.”

Vaccine Development

IT IS GENERALLY AGREED THAT A SAFE, EFFECTIVE, AND WIDELY AVAILABLE preventive HIV vaccine is necessary to bring the HIV epidemic under control. This is particularly true in countries like China, where epidemiologic trends look terribly bleak and the existing health-care infrastructure is simply not prepared to care for millions of HIV-positive residents.

In recent years, Dr. Ho has been working closely with associates at the Aaron Diamond AIDS Research Center in New York and, in Beijing, at the Chinese Academy of Medical Sciences. “We’ve been looking into the subtypes of HIV in China to better understand the epidemic and what we might achieve in developing a vaccine,” Dr. Ho said. “What we’ve found has been encouraging.”

Dr. Ho and his colleagues have been analyzing blood specimens collected from numerous HIV-positive patients from all over China. Not surprisingly, the distribution of various HIV subtypes—subtypes A, B, C, and G have all been documented—is closely related to the mode of viral transmission in the geographical regions studied. For example, in the Yunnan province and the Guangxi Zhuang and Xinjiang Uygur Autonomous Regions, where intravenous drug users account for the majority of the HIV-infected populations, HIV subtype C is dominant. “The viral strains found in these three areas are quite homogenous, which tells us that we’re dealing with a common source of the epidemic and that the epidemic is quite recent,” Dr. Ho said. In the Henan, Hubei, and Shanxi provinces, where blood transfusion/contamination is the major mode of transmission, HIV strains identified consist of highly related subtype-B viruses. “Basically,” Dr. Ho said, “We’re seeing a high degree of viral homogeneity. This finding is consistent with the epidemiology. More importantly, homogeneity could be a significant advantage in developing a vaccine—the less diverse the virus population, the more likely it is we’ll be able to develop an effective vaccine.”

The vaccine strategy being explored by Dr. Ho and his



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Figure 2. This early 2001 file photo shows fourteen-year-old Gao Li (left) and her brother Gao Yan, 11, who were left to fend for themselves after their father (center) died from AIDS in August this year. The children, whose mother also died from AIDS last year, are left to fend for themselves in their village in Gulu township, Henan Province, where they have received little assistance from the government even as villagers continue to die rapidly from selling blood to collection stations which used unsanitary methods in the mid-1980s to 1990s.



Figure 3. Dr. Ho at a signing ceremony in Beijing, at which a prime-boost HIV vaccine initially developed by the Aaron Diamond AIDS Research Center (ADARC) was officially donated to the people of China. The vaccine strategy being explored by Dr. Ho and his colleagues focuses on HIV subtype C, the dominant strain in the Guangxi Zhuang and Xinjiang Uygur Autonomous Regions, where intravenous drug users account for the majority of the HIV-infected populations.



Figures 4a and 4b. Men and women at a drug-rehabilitation center in China. Individuals are self-enrolled or enrolled by their families into these programs. Most are intravenous drug users and approximately half are believed to be infected with HIV (many are tested upon entering the drug-rehabilitation program but few are told their results). “The idea we have would be to enter the camps, provide education and counseling, and follow the HIV-positive individuals once they leave the drug-rehabilitation center,” Dr. Ho explained. “These are individuals who are potential candidates for treatment. We can also learn a lot about the spread of HIV and seroprevalence rates in various communities by following these individuals once they leave the center. With treatment, education, and counseling, the incidence of HIV could actually decrease.”

colleagues focuses on HIV subtype C. It is a prime-boost vaccine—DNA priming followed by a recombinant modified vaccinia Ankara (rMVA) booster—and contains the HIV gag, pol, env, and nef-tat genes. “This is what we wanted—numerous viral components to incorporate into our vaccine vectors,” Dr. Ho explained. “Many of the vaccines currently in development generally involved the incorporation of one or two genes. Just in the way we attack the virus using combination antiretroviral treatment, we now want to develop vaccines that mediate their effects through the induction of immune responses against multiple viral components. This makes a great deal of sense. It’s the best strategy to preclude viral escape.”

At the present time, the design and construction, technical refinements, and immunogenicity studies in animals have been completed for both the DNA and rMVA components of the vaccine. GMP production of the DNA vaccine has been completed and the production for rMVA is currently under way. Safety studies of these vaccines in animals are now in progress. Phase I clinical trials are expected to begin soon and will be enrolling patients in both the United States and China. If all goes according to plan, phase II studies evaluating the DNA component of the vaccine will be initiated in China in 2004; the rMVA component will be tested in 2005. Finally, phase III studies will kick off in China sometime in 2005 or 2006.

Why China for this intensive vaccine efforts? “We have a long-standing relationship with the Chinese Ministry of Health, the Chinese Academy of Medical Sciences, and the Yunnan Provincial Centers for Disease Control,” Dr. Ho explained. “This makes for a strong collaborative effort. There is also a reasonable infrastructure and growing political will in China to realize the vaccine effort. Plus, China has a strong track record in vaccination efforts. And with the increasing rates of HIV infection in select regions, compounded by the relative homogeneity of the predominant HIV strain, this is an opportunity that we must follow.”

Studies are to be conducted in the Yunnan province, with a central clinic, virology laboratory, and immunology laboratory in the capital city of Kunming. Field stations and laboratories have been set up in the cities of Ruili and Mangshi. “Ultimately, if we reach Phase III studies, we’re looking to enroll up to 10,000 subjects in high-incidence, poor areas. This could mean 300 subjects at 33 sites or 1,000 subjects at ten sites,” Dr. Ho said. “We really do have some work cut out for us. We’re gaining a lot of political support, which is necessary if these trials are to be con-

ducted. We’re also in the process of training personnel, both locally and from Beijing. Another component is to provide education and treatment. Fortunately, we’ve been able to secure treatment for some patients from the pharmaceutical industry, which certainly helps build trust. Finally, we will continue conducting cohort studies and molecular epidemiological surveys. This will help support our research agenda and allow us to keep an eye on the course of this epidemic.”

Conclusion

AN EFFECTIVE SUBTYPE-C HIV VACCINE IS JUST ONE OF THE MANY responses that are desperately needed to curtail the mushrooming HIV epidemic in China. Whether it’s strengthening the medical infrastructure to support the timely diagnosis, clinical care, and treatment of HIV-infected people throughout China, or the development of sound prevention programs and messages to slow the spread of HIV, the response needs to be widened and involve multiple government and non-government sectors at all levels: international, national, provincial, and local.

The fact is, HIV has not yet spread widely among all Chinese provinces and autonomous regions. However, countries with nascent epidemics cannot assume that they will never be affected; every country that now has a generalized AIDS epidemic went through a phase of denial that gave the virus time to gain a foothold. Now is the time to act. Before the potential catastrophe in China becomes very much a reality. 

References

Guangxi Epidemic Station. *Year 2000 Annual Report*. Ministry of Health, 2001.
 Ministry of Health Centre for AIDS Prevention and Control, and National Centre for STD and Leprosy Control. *China Annual Report on STD/HIV Surveillance 2000*. Ministry of Health, 2001.
 UN Theme Group of HIV/AIDS in China. *2001 Update of the AIDS Situation and Needs Assessment Report*. UNAIDS, 2002.