

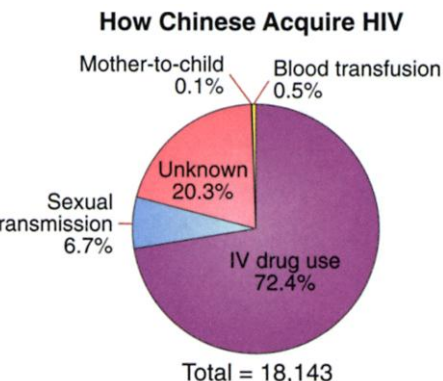
## INFECTIOUS DISEASES

# China Awakens to Fight Projected AIDS Crisis

An increase in drug use and a boom in commercial sex have led China to the brink of an AIDS explosion. But its historic isolation also gives the country an advantage in testing the latest vaccines

**BEIJING**—China is poised to become the next AIDS battleground. The country has so far escaped the global HIV/AIDS onslaught: The official tallies count only 670 confirmed AIDS cases and 18,143 confirmed HIV-infected people among the 1.2 billion population. But by all indications, the epidemic is about to sweep through the world's most populous nation with a vengeance. The real number of infected people probably tops 500,000, according to China's National Center for AIDS Prevention and Control (NCAIDS), an estimate that has risen fivefold since 1996 based on increasing intravenous drug use, changing sexual mores, and a burgeoning commercial sex industry. If current trends continue, NCAIDS projects that China could have 10 million HIV-infected people by 2010.

"If China does not take effective measures, AIDS will become a national disaster," virologist Zeng Yi, former head of the Chinese Academy of Preventive Medicine in Beijing, warned in a recent report to the Chinese Academy of Sciences. The cost of treating AIDS patients and the lost productivity, he says, could "ruin the economic gains China has made" since the mid-1980s.



**Testing, testing.** Three multinational teams (*right*) are planning trials in China of vaccines to prevent AIDS, now contracted mainly through intravenous drug use (*above*).

One ray of sunlight in this dark picture is that China may be one of the best places to test AIDS vaccines. Researchers hope that getting an early start, before dif-

ferent HIV strains commingle, will make it easier to find concentrated populations suitable for testing vaccines aimed at specific subtypes of the virus. And China's well-developed public health infrastructure could help facilitate those trials.

In addition, Zeng says he's "encouraged" by the recent actions of national leaders, who he says were initially slow to react. The 2-year-old NCAIDS, part of the Academy of Preventive Medicine and funded by the Ministry of Health, has expanded the academy's activities by supporting epidemiological studies and a behavioral intervention unit. It has also been promised a new building, and the state-controlled media have given high-profile coverage to the topic. China's increased activity not only benefits its own population, notes Wayne Koff, vice president for research and development at the International AIDS Vaccine Initiative (IAVI) in New York City, but "it also will complement ongoing [global] efforts by IAVI and others."

Yet the overall level of spending in China remains woefully low. China's national

Even a bigger budget can't overcome some structural problems, however. Wu Zun-you, NCAIDS's director of behavioral intervention, says he has not been able to establish needle-exchange programs for IV drug users or distribute condoms to commercial sex workers because the government views such efforts as condoning illegal activity. And many local officials are still unaware of the need to act. "Even with a national mandate, without local support it's very difficult to carry out effective intervention," says Wu.

AIDS education efforts are also hampered by the fact that most public health workers are hired and paid by local governments. And although many localities are actively supporting HIV/AIDS prevention activities, others are not. Zeng says some regional officials are probably underreporting cases to cover up lax supervision of such things as blood collection and to avoid scaring off foreign investors. Wu adds that police in some areas still arrest women carrying condoms on suspicion of prostitution, despite national campaigns that emphasize their legitimate public health role. As a result, Wu says, education efforts must be aimed at local officials as well as the general population. "But progress is not quick enough to match the speed of the epidemic," he says.

## Opening the gates

Zeng says China's leaders initially were lulled into complacency by the low number of actual AIDS cases and what was, until recently, a low estimated rate of infection. "The problem looked very small, given the 1.2 billion population," he says. The HIV/AIDS problem

## PLANNED VACCINE TRIALS

Province	Xinjiang	Yunnan	Guangxi
Partners	U. Regensburg, Germany/NCAIDS	Rockefeller U., New York/NCAIDS	Johns Hopkins U., Baltimore/CNIDA
Funder	European Union (EuroVac)	IAVI	U.S. NIAID
Type of Vaccine	DNA vaccine	DNA vaccine	DNA vaccine
HIV clade	B/C recombinant	C	B/C recombinant
Start	Early 2001	Late 2001	2001–02

government now spends just 15 million yuan (\$1.75 million) on HIV/AIDS programs, although officials hope that number will quadruple in the next fiscal year. Provincial and local governments also spend a small but unknown amount. And although other countries and international agencies such as the Joint United Nations Programme on HIV/AIDS and the World Bank are beginning to provide funds, their support only scratches the surface.

came late to China because of its limited contacts with other countries, the government's strict enforcement of antidrug and antiprostitution laws, and culturally conservative attitudes about sex in general.

But the accelerating economic reforms and increasing contacts with the rest of the world have opened up the same HIV infection routes in China that have plagued other countries. First among these is growing intravenous drug use, particularly along

China's southern and western borders, and sharing of needles. A 1999 estimate by China's State Antidrug Commission of 680,000 drug users represents a 14% increase in the past year. About 72% of the 18,000 confirmed HIV-infected people are IV drug users (see pie chart).

More worrisome to public health officials is an increasingly sexually active population, at least as measured by the rise in commercial sex and sexually transmitted diseases (STDs). Although heterosexual transmission accounts for only 6.7% of HIV infections, the number of reported STDs has doubled in the last 2 years, to more than 800,000 cases in 1999. Qu Shuquan, deputy director of epidemiology at NCAIDS, says that the actual number of new cases is probably three to five times higher because the country's surveillance network doesn't cover private clinics.

The return of STDs is a dramatic turnabout in a country where such health problems were rarely seen in the 1960s. Wu says today's Chinese are throwing off old sexual taboos. "Having multiple sex partners [over the course of a lifetime] is not necessarily considered immoral anymore," he says. And migrant workers are compounding the problem. The collapse of state-owned enterprises has forced rural men to seek work in the coastal cities, where the commercial sex trade is flourishing.

Finally, China seems to be sitting on an HIV time bomb triggered by tainted blood. Much of the problem can be traced to poor, rural Chinese who sold blood or plasma to commercial collection centers. A 1999 study in a small village in Henan Province found that 80 of 140 residents who had sold blood or plasma had contracted HIV, presumably through inadequate sterilization procedures at a commercial blood collection center. They are not included in the official tally of persons who contracted HIV through blood transfusions, however, because that category includes only recipients of tainted blood.

In 1998 the government banned paid blood "donations," closed a number of commercial blood collection centers that didn't meet safety standards, and introduced screening. But regional newspapers have reported that many donors continue to be paid because of a dearth of volunteers.

#### Local trials

While public health officials struggle with preventive strategies, researchers are emphasizing the need to boost the country's basic epidemiological and biomedical research capabilities. Shao Yiming, a virologist and deputy director of NCAIDS, says that biomedical research now receives about 5% of the government's HIV/AIDS budget, a proportion he hopes will be maintained as

the total budget rises. He also hopes to convince the Ministry of Science and Technology to start funding HIV/AIDS-related research that would complement work supported by the Ministry of Health.

Another goal is to steer at least a small portion of the international aid now going into education and prevention into research to build China's scientific capacity. Researchers here are particularly excited about



**Shaping behavior.** Wu Zunyou holds a poster warning intravenous drug users of the dangers of dirty needles.

a new U.S. National Institutes of Health grant program that will be open to HIV/AIDS researchers based outside the United States (*Science*, 2 June, p. 1563). Such grants will "help fill the gap" in funding for basic research in China, Shao says. He says HIV/AIDS efforts in other developing countries have suffered when nonresident researchers leave at the end of their project, so it is particularly important for Chinese scientists to be involved in developing vaccines and treatments that are affordable. "We do not want to see a vaccine developed that is just a rich-country vaccine," he says.

China's indigenous research capabilities and the state of its HIV/AIDS epidemic, in fact, help make the country a promising location for vaccine trials. For one, Shao notes that the incidence of new infections in much of the developed world has plateaued. "If you try a vaccine in a region with low incidence of new infections, you need a huge cohort to show statistically significant efficacy," he says. With new infections still rising in China, vaccine trials could be based on smaller cohorts and yield quicker results, he says.

Hans Wolf, a virologist at the University of Regensburg in Germany, who is working with NCAIDS on an upcoming trial in Xinjiang, adds that each subtype of HIV is likely to require its own vaccine, much as influenza vaccines must be updated for each new outbreak. Other researchers are hopeful that a single vaccine will eventually prove to work against different subtypes, or clades, of the

virus. But to reduce the variables involved, many HIV vaccines now in the works target a particular clade and will be tested in regions where that clade predominates.

Xiao-Fang Yu, a molecular biologist at Johns Hopkins University in Baltimore, says that variation even within clades is less in China than in other countries. In 4 years of studies of the B/C recombinant strain of HIV that is common in Guangxi Province,

samples from five regions have turned up just 1% to 2% variation in the genetic sequence of the HIV envelope protein. In contrast, he says, there can be as much as 15% to 20% variation in samples taken from just two patients in Baltimore. "If [developing] a vaccine depends on the homogeneity of the virus, then China will be an ideal place for that vaccine trial," he says. The homogeneity of the virus in China "at least allows you to test whether some of the [vaccine] strategies have any efficacy under the most ideal situation."

A final factor is what David Ho, director of the Aaron Diamond AIDS Research Center of Rockefeller University in New York City, calls China's "reasonable infrastructure." A well-established hygiene and epidemic surveillance network that has defined the number and distribution of the different HIV strains also can support the kind of cohort studies required for vaccine trials. After 3 years of preparatory effort, Yu's group just recently set up China's first HIV/AIDS cohort study based on 700 IV drug users in Guangxi Province. "This will be very significant in determining if the location is suitable for phase III efficacy trials," he says.

China's epidemiological and infrastructure advantages have attracted several groups (see table), all of which are planning to test vaccines that contain HIV genes stitched into a stretch of DNA called a plasmid. Although Wolf says he would prefer to see greater variety, IAVI's Koff notes that these tests will complement trials elsewhere of other types of vaccines.

Although Zeng supports vaccine development, he says that its long time horizon demonstrates the need for other, short-term strategies to combat HIV/AIDS. "Maybe within 10 years we'll have a vaccine," Zeng says. But until then, "the most urgent [need] is for nationwide education and intervention."

—DENNIS NORMILE

With reporting by Justin Wang and Li Hui of *China Features*.