2005

Association of plasma donation with human immunodeficiency virus and hepatitis C virus infections in rural Shanxi Province, China.

Han-Zhu Qian
University of Alabama at Birmingham

ASSOCIATION OF PLASMA DONATION WITH HUMAN IMMUNODEFICIENCY VIRUS AND HEPATITIS C VIRUS INFECTIONS IN RURAL SHANXI PROVINCE, CHINA

by

HAN-ZHU QIAN

A DISSERTATION

Submitted to the graduate faculty of The University of Alabama at Birmingham,
in partial fulfillment of the requirements for the degree of
Doctor of Philosophy

BIRMINGHAM, ALABAMA

2005

ABSTRACT OF DISSERTATION
GRADUATE SCHOOL, UNIVERSITY OF ALABAMA AT BIRMINGHAM

Degree Ph.D. Program Epidemiology

Name of Candidate Han-Zhu Qian

Committee Chair Sten H. Vermund

Title Association of Plasma Donation with Human Immunodeficiency Virus and Hepatitis C Virus Infections in Rural Shanxi Province, China

Illegal commercial plasma donation activities in the late 1980s and early 1990s caused many HIV and HCV infections in rural China due to the use of unsterilized equipment and reinfusing pooled red blood cells to donors. A review of the HIV/AIDS epidemic in China showed that sub-groups at higher HIV risk are shifting from injection drug users and former plasma/blood donors to female sex workers and their clients, and men who have sex with men. Updated data on the prevalence of HIV and HCV, and HIV/AIDS knowledge and attitudes in the communities with donors are sparse.

Analysis of the data from 524 randomly selected adult villagers in 12 villages (pilot study) showed that the knowledge of HIV transmission routes and prevention was fairly good, but misconceptions were also common. Discriminatory attitudes were prevalent and were independently associated with lower knowledge of HIV/AIDS, lower education, older age, and married status. HCV seroprevalence rates were 8.2% in all participants, 27.7% in donors, and 2.6% in nondonors. Selling blood or plasma was the strongest predictor for HCV seropositivity (OR=14.4; 95% CI: 7.1-31.6). Receiving a blood transfusion was also independently associated with HCV (OR=8.3, 95% CI: 2.1-32.0). Plasma donors had higher risk than whole blood donors (OR=7.6, 95% CI: 2.9-20.9).

Analysis of the data from 3062 villagers in 4 villages (main study) showed that

29.5% reported to be former blood or plasma donors, 8.3% had ever sold plasma alone. HIV seoropositivity was confirmed in 1.3% of subjects, while 12.7% were HCV sero-positive. HIV-HCV coinfection rates were 1.1% in all, 85% in HIV positive, and 8.7% in HCV-positive subjects. Factors associated with coinfection were residence in a village with a prior plasma collection center (OR=2.7, 95% CI: 2.1, 3.5), male sex (OR=7.7, 95% CI: 3.8, 15.8), older age (OR=1.6, 95% CI: 1.2, 2.0), lower education (OR=1.4, 95% CI: 1.1, 1.8), a history of selling plasma (OR=14.1, 95% CI: 10.5, 18.9), and having a spouse infected with HIV or HCV.

In conclusion, HCV coinfection should be considered in HIV intervention projects. Community education to eliminate misconceptions and increase knowledge may help reduce HIV/AIDS stigma and discrimination.

DEDICATION

This work is dedicated to my wife, Guilan Liu, for her love, support, and patience, and to my son, Frank Qian, for his understanding. My wife took good care of our family without any complaints during my nearly 5-year study. She endured over one year of loneliness and sometimes fear when I went to China for the project and lived in the epi-center of the SARS epidemic! My son learned to postpone his gratification at his very young age and allowed me to indulge myself in the dissertation work while ignoring him. Your love makes this work the most precious gift of mine for you.

ACKNOWLEDGMENTS

I am deeply grateful to my advisor, Dr. Sten H. Vermund, for his superb mentoring. He instilled in me his high academic vision, taught me to insist on facts, brought me into his broad academic networks, and gave me football tickets and encouraged me to enjoy American culture. I have learned much and grown much in my time as his apprentice.

Many thanks to my advisory committee: Drs. Eric Chamot, Huey Chen, Christopher S. Coffey, and Richard A. Kaslow. They always gave quick replies to my questions even though they had their own busy schedules. Their thoughtful advice facilitated the process of completing this work. My experience as a teaching assistant with Dr. Kaslow is also very helpful for this work and for my future career. A special thanks also to Dr. Ellen M. Funkhouser, the Ph.D. program director, who provided much help to me during these years of study.

I thank Drs. Yiming Shao, Ning Wang, and Xiwen Zheng at the Chinese Center for Disease Control and Prevention for their generosity in allowing me to use the data, and thank Drss Zhongmin Yang, Xiaoming Shi, and Jianghua Gao for collecting the data.

It would not have been possible to complete this work without financial aid from the UAB Department of Epidemiology and the UAB/Fogarty International Research Training Programs, and without consistent support from many faculty and staff in the Department of Epidemiology.

I would like to acknowledge Ms. Becky Brazeel for her kind help in fitting my appointments in Dr. Vermund's busy schedules. I thank Dr. Mirjam C Kempf, Dr. Hong Cheng, Ms Ilene Brill, and my fellow doctoral students Drs.Thomas J. Bender, Madhav P. Bhatta, Ronald Cantrell, Yujiang Jia, Christopher Krawczyk, Jian Li, Qing Li, Kayvon Modjarrad, Mustafa Mohd, Chengbin Wang, Yan Xiao, Mingwei Xu, and Shiming Zheng, for sharing their brilliant ideas and knowledge with me.

All of this support and friendship will always be cherished.

TABLE OF CONTENTS

Page

LIST OF TABLES

LIST OF TABLES (Continued)

LIST OF FIGURES

Figure *Page*

LIST OF ABBREVIATIONS

AIDS	acquired immunodeficiency syndrome
ARV	antiretroviral
CSW	commercial sex worker
CI	confidence interval
FPD	former plasma donor
HCV	hepatitis C virus
HIV	human immunodeficiency virus
IDU	injection drug user
MSM	men having sex with men
MTCT	mother-to-child transmission
OR	odds ratio
STD	sexually transmitted disease

INTRODUCTION

As the most populous country in the world, China faces a potential explosion of the human immunodeficiency virus /acquired immunodeficiency syndrome (HIV/AIDS) epidemic, as the Joint United Nations Programmme on HIV/AIDS (UNAIDS) warns. However, a very limited published literature on HIV/AIDS in China has emerged in English thus far, mainly due to the language barriers, international communities are not able to fully understand the whole picture of the HIV/AIDS problem in China. Moreover, there is a great discrepancy between officially reported cases and the estimated infections: over 60 thousand cumulative cases versus 1 million estimated infections through the year 2003. The international community has criticized the Chinese government for covering up the problem. A lack of correctly analyzed and interpreted data and sparse communication of the results with the outside world via publication in English-language journals may contribute significantly to the discrepancies in data and the perception by foreigners of a lack of frankness, and may therefore hinder the global collaboration in the control of the AIDS epidemic in China.

We critically review the magnitude of HIV/AIDS epidemic and the social characteristics and geographic distribution of at-risk groups in China based on published literature and unpublished official data, both in Chinese and in English. Key databases included the (1) Chinese Journal of Epidemiology (*Zhonghua Liu Xing Bing Xue Za Zhi)*; (2) national HIV/AIDS case reports 1995-2003; and (3) national HIV sentinel surveillance data 1995-2003.

Contaminated plasma/blood collection practices in the late 1980s and early 1990s caused the spread of several blood-borne diseases in rural central and eastern China, and ranked as the second most important contributor to the HIV/AIDS epidemic in China by 2004. These practices were largely stopped by 1998 by the Chinese government, which closed down the illegal commercial plasma/blood collection centers, enacted a new blood donation law, and required universal HIV screening for blood donors. A small number of previous studies found varying prevalence rates of HIV and hepatitis C virus (HCV) infections in these commercial blood/plasma donating communities; studies on knowledge, attitudes, and behaviors about HIV/AIDS among former plasma/blood donors (FPDs) were even sparser.

The Chinese government has initiated intervention efforts in these former plasma donating communities. Stigma and discrimination against people with HIV/AIDS are one of major barriers to effectively prevent HIV transmission. Understanding the association between discriminatory attitudes and knowledge level will assist in the design of these intervention projects. As more and more HIV-infected FPDs are developing into AIDS cases, antriretroviral (ARV) treatments are urgently needed. HIV-HCV coinfection data will provide valuable information in guiding ARV therapy for AIDS patients and antiviral treatment for HCV patients.

Data used for this study come from an ongoing, 5-year National Institute of Allergy and Infectious Diseases-funded China Integrated Programs for Research on AIDS. A cross-sectional survey was conducted in Shanxi Province, China and included two parts: the pilot study recruited a random sample of adult residents aged 18-59 years in 12 villages, and the main study was a census of residents aged 18-64 years old in 4 villages

that had a higher prevalence of blood donation and HIV infections. A questionnaire-based interview and laboratory testing for HIV and HCV infections were completed for each participant (table 1).

We perform secondary data analysis to estimate the seroprevalence rates and risk factors of HIV and HCV infections among residents in former plasma-donating communities in China, and to test the hypothesis that better HIV/AIDS knowledge predicts fewer discriminatory attitudes towards person with HIV/AIDS.

Table 1. Comparison of pilot study and main study in the cross-sectional study.

Item	Pilot Study	Main Study
Study year	November to December, 2003	May to August, 2004
Study site	12 former plasma donating villages	4 villages with higher prevalence of former blood donation (from pilot study)
Study population (actual analyzed sample)	524 adult villagers age 18-59 years old	3062 adult villagers age 18-64 years old
Sampling method	Random sampling	Census
Questionnaire	"Pilot Study Questionnaire" including HIV/AIDS knowledge and attitudes	"Main Study Questionnaire", excluding HIV/AIDS knowledge and attitudes
Laboratory measures	HIV and HCV	HIV and HCV

RISK OF HIV/AIDS IN CHINA: SUB-POPULATIONS OF SPECIAL IMPORTANCE

by

HANZHU QIAN, STEN H. VERMUND, AND NING WANG

Submitted to *Sexually Transmitted Infections*

Format adapted for dissertation

ABSTRACT

To describe the HIV/AIDS epidemic in mainland China, we review the magnitudes of the HIV/AIDS epidemic and the social characteristics and geographic distribution of at-risk groups in China based on published literature and unpublished official data. Injection drug use has been the dominant route for HIV infection in China and will continue to be a major risk factor, with increasing numbers of new drug users and needle sharing. Commercial plasma donation with unhygienic reinfusion of red blood cells was common in rural communities in early 1990s. While this is unlikely to constitute a major factor in the future spread of HIV, those already infected represent a formidable treatment challenge. Huge seasonal work migration facilitates disease spread across regions. Many homosexual men have unprotected sex with men, women, or both, and may contract or spread HIV. Though commercial sex workers have contributed to a small proportion of the reported epidemic thus far, flourishing commercial sex is of growing concern and may play a bridging role of transmitting HIV from core groups to the general population. Increasing numbers of sex workers and drug users, internal migration, high-risk behaviors, and low condom use suggest future upward trends for HIV/AIDS and underscore the urgency of scaling up interventions in China.

INTRODUCTION

Since the first acquired immunodeficiency syndrome (AIDS) case was diagnosed in 1985, China has reported 62,159 human immunodeficiency virus (HIV)/AIDS cases cumulatively by the end of 2003. The actual number was estimated by the Ministry of Health of China to be nearly one million. As the world's most populous country, China

has a low overall HIV prevalence, with nearly 0.1% infected in the general population (2002) [1]. However, the HIV/AIDS epidemic in China is facing a potential explosion; the rise in reported HIV/AIDS cases was about 30% per year between 1998 and 2002, with a 54% rise from 2002 to 2003 alone. The Joint United Nations Programme on HIV/AIDS (UNAIDS) warned that China could have 10 million infections and 260,000 orphans due to AIDS by 2010 if effective intervention measures were not taken [1].

The HIV/AIDS epidemic in China is largely concentrated in selected areas and population sub-groups. Among 31 provinces, autonomous regions, or municipalities, Xinjiang and Yunnan have the highest prevalence rates of cumulative reported cases, within the range of 30 to 45 per 100,000 people; Guangxi, Beijing, and Henan are within the range of 10 to 30 per 100,000 (figure 1). HIV infection is primarily attributable to injection drug use (IDU) in southern (Yunnan, Guangxi, Guangdong), central-western (Sichuan, Chongqing, Guizhou), and northwestern (Xinjiang) China. Prior illegal commercial blood collection is primarily responsible for infections in Henan, Anhui and Hubei in central-eastern China. Commercial sex is a major contributor in coastal provinces such as Fujian. Migrant populations from higher risk areas accounts for most cases in Beijing and Shanghai [2].

We searched English and Chinese language literature via Medline and the China National Knowledge Infrastructure, and reviewed unpublished official data including national HIV/AIDS case reports and sentinel surveillance data. Over 250 papers and reports were reviewed. Key databases included the (1) Chinese Journal of Epidemiology (*Zhonghua Liu Xing Bing Xue Za Zhi)*; (2) national HIV/AIDS case reports 1995-2003; and (3) national HIV sentinel surveillance data 1995-2003.

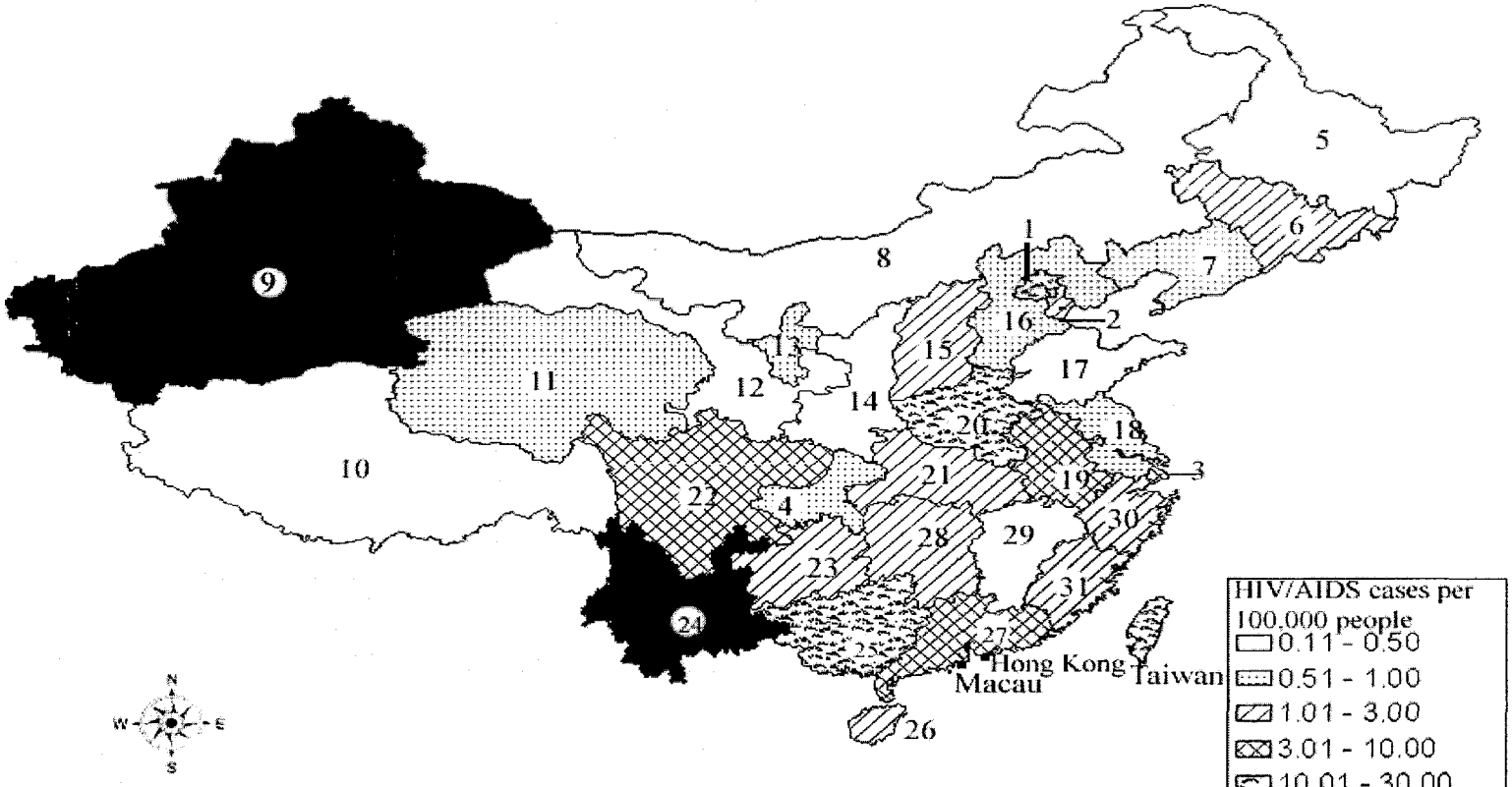

Figure 1. Cumulative reported HIV/AIDS cases in China per 100,000 persons, by region, 1985-2003. Numerators are cumulative cases; denominators are population from 5th National Population Census in 2000. 1-Beijing, 2-Tianjin, 3-Shanghai, 4-Chongqing, 5-Heilongjiang, 6-Jilin, 7-Liaoning, 8-Inner Mongolia, 9-Xinjiang, 10-Xizang (Tibet), 11-Qinghai, 12-Gansu, 13-Ningxia, 14-Shaanxi, 15-Shanxi, 16-Hebei, 17-Shandong, 18-Jiangsu, 19-Anhui, 20-Henan, 21-Hubei, 22-Sichuan, 23-Guizhou, 24-Yunnan, 25-Guangxi, 26-Hainan, 27-Guangdong, 28-Hunan, 29-Jiangxi, 30-Zhejiang, 31-Fujian. Hongkong (31.68/100,000 persons), Macao (64.23/100,000 persons).

INJECTION DRUG USERS (IDUs)

Opium use was popular from late Qing Dynasty (1644-1911 A. D.) to the founding of new China in 1949, and was almost eradicated after the early 1950s. Drug use re-emerged in the late 1980s, increasing from 70,000 registered drug users in 1990 to 1 million by 2002 (table 1) [3]. China's southwestern border with the "Golden Triangle" region of Southeast Asia (including Myanmar, Laos, and parts of Thailand) is proximate to one of the major heroin-producing areas in the world [3]. Three drug trafficking routes enter China, two through Yunnan province from Myanmar and one into Guangxi province from Vietnam. These drug trafficking routes then run across several provinces in

Table 1. Sub-group populations at higher risk of HIV/AIDS in China.

Population	Registered / estimated number (million)	Reported % of HIV/AIDS cases (%), 1985-2003 [a] (*N*=62,159)	Estimated % of people living with HIV/AIDS in 2003 [b] (*N*=840,000)	Average HIV prevalence (range) (%)
Injection drug users	1.0 / 3.5 [c]	51.2	43.9	7.0 (0-94.0) [c]
Former plasma donors	NA	21.0	24.1	NA (0.2-56.1)
Commercial sex workers	0.4 [e] / 3.5 [f]	7.3 *	19.8 *	1.0 (0-11.3) [d]
Men who have sex with Men	NA / 8.0 [g]	0.2	11.1	NA (0-3.1)
Others	NA	20.3	1.1	NA
Total	NA	100.0	100.0	0.1 (0.1-0.2) [h]

NOTE. NA: data not available. * including their clients and other people infected via heterosexual transmission.

[a] Ref # 2. [b] Joint assessment by State Council AIDS Working Committee Office and UN Theme Group on HIV/AIDS in China, 2004. [c] National Drug Abuse Surveillance Center, 2002. [d] Ref # 7. [e] Public security report in 1996. [f] UNAIDS China (1997): China responds to AIDS: HIV/AIDS situation and needs assessment report.. [g] Ref # 47. [h] among general population age 15-49 years (end 2003), estimate from UNAIDS: 2004 Report on the global AIDS epidemic.

southwestern, southern, and northwestern China, including Yunnan, Guangxi, Guizhou, Guangdong, Sichuan, and Xinjiang [4]. Along these routes and beyond, some drug smugglers and local residents have become drug users. The major drugs of choice are heroin and opium; the abuse of amphetamine-type stimulants and methylenedioxymethamphetamine has recently become popular in growing urban areas [3, 5].

National behavioral surveillance data suggest that injection is an increasingly common route for illicit drug use as a cost-effective way of experiencing the effects of the drug, compared to noninjection [6]. The average prevalence of IDU among drug users increased from 35% in April 1995 to 61% in April 2003 [7]. Among IDUs, about 45% share needles [7].

The relationship between drug trafficking, drug use, needle sharing, and HIV spread has been well documented in China [8, 9]. HIV infection among IDUs began around 1988 in Thailand and Myanmar [10, 11]. Analysis of HIV virus subtypes suggests a spread from the "Golden Triangle" region to the Yunnan Province [4, 12], and then further to other parts of China along the drug trafficking routes [4, 12-14]. The first HIV outbreak in China was reported in 1989 among IDUs in Ruili city of Yunnan province, bordering Myanmar [8]. By 1995, 12 of the 17 prefectures in Yunnan reported HIV infection [15]. By 1999, the average prevalence of HIV infection among IDUs from sentinel surveys was 27.8% [16]. The HIV epidemic in Guangxi (east of Yunnan) began in 1989 and accelerated markedly in the years after 1996; more than 500 new cases were reported each year after 1998 [17]. By 2000, 88% of cumulative HIV/AIDS case reports were due to IDUs [17]. In Guangdong, HIV began to spread among IDUs in 1997; during 1986-1996, 1.4% of locally reported HIV/AIDS cases were local resident IDUs, but this pro-

portion increased to 73.3% in 1999 case reports [18, 19]. In Xinjiang, HIV prevalence among IDUs increased from 0% in 1995 to 28.8% in 1998 in the capital city Urumqi, and was 82.2% in Yining City in 1998 [6]. High HIV prevalence rates were observed later in selected sentinel sites for IDUs in other provinces, e.g., Jiangxi (14.5%, 2000 sentinel data), Sichuan (16%-20%, 2002), Guizhou (17%-19%, 2002), and Hunan (15%-20%, 2003) [7].

Although the proportion of reported HIV/AIDS cases attributable to IDU decreased from 71% during 1985-2000 to 50% in 2002 [2], HIV prevalence among IDUs increased. In 1995, only 1 out of 8 national sentinel sites for IDUs detected HIV infections, while in 2002, 29 out of 36 sentinel sites did; the average prevalence rates among drug users increased from 0.04% in 1995 to 5.9% in 2002 (table 2) [7, 20].

FORMER PLASMA DONORS (FPDs)

In general, people in China are reluctant to donate blood, as they believe that the loss of blood is unhealthy. In 1996, only 11% of blood for clinical use was collected from volunteer donors nationwide, although this proportion increased to 67% in 2000 due to vigorous efforts by the government to motivate volunteer donors [21]. More than 90% of whole-blood donations collected in China are only in 200-mL volumes, in contrast to the Western tradition of 400-500 mL per donation [21]. Endemic hepatitis also limits voluntary blood donation from a large proportion of the general population because the blood is discarded when screened and found to be positive for hepatitis B surface antigen or hepatitis C antibody. A shortage of blood products in China led to a large market for

Table 2. National Sentinel surveillance of HIV/AIDS among selected populations in China, 1995-2002.

	October, 1995	October, 1998	October, 2002
Among injection drug users			
Sites with >1 positive HIV test / Surveillance sites	1/8	11/19	29/36
Positive persons / Persons tested (%)	1/2652 (0.04)	285/5536 (5.2)	570/9713 (5.9)
Prevalence at sites (per 100 persons) Lowest / Median / Highest	0 / 0 / 0.25	0 / 0.3 /82.2	0 / 2.5 / 80.0
Among commercial sex workers			
Sites with >1 positive HIV test / Surveillance sites	1/12	4/21	4/31
Positive persons / Persons tested (%)	1/3160 (0.03)	29/5052 (0.57)	103/7507 (1.37)
Prevalence at sites (per 100 persons) Lowest / Median / Highest	0 / 0 / 0.3	0 / 0 / 4.5	0 / 0 / 15.9
Among sexually transmitted disease patients			
Sites with >1 positive HIV test / Surveillance sites	1/15	5/35	16/56
Positive persons / Persons tested (%)	1/4734 (0.02)	8/10441(0.08)	26/10070 (0.26)
Prevalence at sites (per 100 persons) Lowest / Median / Highest	0 / 0 / 0.3	0 / 0 / 0.7	0 / 0 / 2.5

NOTE. Data were abstracted from references 6 and 21, and national sentinel surveillance report in 2002. Median values of 0 indicated that >50% of sites did not identify any infected persons.

illegal commercial plasma/blood collections in the late 1980s and early 1990s. Hundreds of commercial plasma collection centers were established in counties, townships, and villages in central-eastern China. The paid donors were generally farmers from poorer areas who sold plasma or blood to augment their incomes [22, 23].

Plasma donation was much more popular than whole blood donation for three reasons: (1) increased commercial demand for plasma; (2) increased willingness to donate when red blood cells were reinfused; (3) repeat donations could be solicited in a short time period when anemia was reduced with red blood cells reinfusion. Typically, peripheral blood was drawn from several people at the same time. Donations sharing the same blood type were mixed together in a container and the plasma was extracted. Red blood cells were reinfused with normal saline solution to the donors. Such procedures, along with the reuse of needles and unsterilized equipment, gave endemic blood-bone infections an easy route to spread rapidly through the local donor population [22, 23].

Blood screening for HIV for all donors was required by law in large cities after 1993, but local blood banking or hospital officials often omitted HIV testing both for financial reasons and because they believed they did not have an HIV problem. Begining around 1995, the problem of HIV spread among commercial plasma donors began to become apparent [24, 25]. The Chinese government took strong legal action to prevent the further spread of HIV infections by closing commercial plasma collection centers and issuing new regulations for blood/plasma donation. In 1998, the Law of Blood Donation became effective nationwide, encouraging voluntary donation and requiring HIV screening for all blood donations. Although it was believed that illicit commercial blood/plasma

collection has been reduced substantially since 1996, the practice has been occasionally reported in the mass media and it has not been completely eradicated [26].

There are no official data on the number of commercial blood donors given the illegality of the practice. However, several provinces in central and eastern China, such as Henan, Hubei, Anhui, Shanxi, Hebei and Shangdong, were believed to have an especially large number of blood donors [24, 27-31]. By 2003, 21.0% of cumulatively reported HIV/AIDS cases in China were attributable to these flawed blood collection methods (table 1).

HIV/AIDS prevalence rates varying from 0.2% to 56.1% among paid blood donors have been reported in village surveys where commercial blood banking was documented [29, 32-34]. Plasma/blood donation was the strongest predictor of HIV infection in these communities; in one study, 17.0% prevalence was observed among donors, compared to 0.2% among nondonors [34]. Donors aged 30-49 years had nearly twice the risk of other age groups [22]. Only selected types of blood banks were likely to be responsible for the HIV epidemic among former plasma donors, namely private or local county government blood banks; the district government and military blood banks were not associated with HIV risk in one study [35]. Plasma donors had a higher prevalence rate (25.9%) than those who donated whole blood (2.6%) [35]. Donors who donated blood $\geq$10 times per year had a higher prevalence rate (13.5%) than those who donated <10 times a year (2.8%) [28]. The prevalence rates for blood donors were 18.3% if they donated before 1995, 7.7% if they donated beginning in 1995-1996, and 1.4% if their donation began after 1996 [28]. While it is plausible that these observations are generalizable, they are derived from relatively geographically limited surveys within a vast country.

COMMERCIAL SEX WORKERS (CSWs) AND THEIR CLIENTS

Prostitution was very common in the large trading cities of China in the late 19th and early 20th centuries [36]. It was abolished by 1955 after a national campaign against prostitution and venereal diseases based on changing social mores, closing brothels, and educating and training CSWs for other employment [37]. Since adopting a free market economy and an open door policy in 1978, China has experienced rapid economic growth, far more in coastal areas and big cities than the inland rural areas. Mass migration of rural inland people to coastal cities for job opportunities, widening income gaps, increased business and tourism travel, and more tolerant sexual attitudes have led to widespread commercial sex. The number of sex workers identified by public security departments increased from 25,000 in 1986 to 250,000 in 1992, and to 420,000 in 1996 [38]. The actual number involved in commercial sex is estimated to be 3 to 4 million persons [39]. Among Chinese men age 20-64 years old, 6.4% have engaged in commercial sex at least once during their lives, according to a nationwide population-based probability survey in 2000 [40]. Condom use in commercial sex is not widespread. According to national behavioral sentinel surveillance data, the median proportion of those reporting always using condoms showed a slowly increasing trend, from 13% in 1995 to 20% in 2002 [7].

Much remains to be learned about CSWs in China. Brothels are a far less common phenomenon than in nearby Asian countries [41]. Transient sex work is common, such that girls or young women will work in "hairdressing salon", "song bars", bathing centers, hotel bars, dance halls, or from the street for a relatively limited time (a few months to a few years). Their goal is to save a "nest egg" for starting a small business or helping financially troubled parents [42, 43]. To maintain relative anonymity, it is com-

mon for CSWs to work away from their hometowns. Other major motivations to enter prostitution have included negative sexual or love experiences and, in a small minority, self-reported enjoyment of sex work [43, 44]. While a majority of women involved in commercial sex are thought to be of rural origin, women laid off from state-owned factories and even women who are fully employed are represented among CSWs. These women may work part-time at night and weekends to make extra income. Given the wide variety of sex work, it is hard to generalize to their HIV-related behaviors. Male prostitution is said to exist but it is rarely seen. The dynamism of modern China suggests the need for ongoing behavioral surveillance to track risk behaviors and trends in CSWs.

Along with the growth of commercial sex and a continued low rate of condom use, the incidence rates of sexually transmitted diseases (STDs) have increased sharply since the 1980s. Among 8 reportable STDs in the whole country, only 50 cases were reported in 1980, 160,000 in 1990, and 850,000 in 2000 [45, 46]. Many Chinese physicians had virtually no clinical experience with STDs prior to the 1990s. HIV prevalence rates among STD patients and CSWs show upward trends, and sentinel data in STD clinics documented this association. Average prevalence among STD clients and CSWs increased from 0.02% and 0.03% in 1995 to 0.08% and 0.57% in 1998, and further to 0.26% and 1.37% in 2002, respectively (table 2) [7, 20]. While these HIV prevalence rates are not high by global standards, the upward trend is worrisome. Through 2003, heterosexual transmission accounted for 7.3% of cumulative reported HIV/AIDS cases in China (table 1).

OTHER SUB-POPULATIONS AT RISK

Migrant People

China has 100-120 million people who travel away from their homes for work each year [47]. Migrant women of rural origin often lack good education and job skills, and may have limited opportunities to earn money; an increasing number of young women are recruited into sex work [47, 48]. Migrants are largely young and sexually active; migrant males are likely to become clients of commercial sex workers when far from home and with increased disposable income. Migrants present special challenges for HIV/STDs prevention because of these commercial sex links, prior frequency of commercial plasma/blood donation, and a higher prevalence of drug and alcohol use. Migrants may spread HIV and STDs between rural and urban areas as well as from HIV concentrated regions to low-prevalence regions. A convenience sampling of migrants in Beijing and Shanghai showed that 47% (85/180) of the employment seekers reported engaging in extramarital sex since leaving their place of origin, higher than restaurant workers (16%, 5/32) and peddlers (14%, 22/192); migrant employment seekers also had a high prevalence of selling blood or plasma and drug use (12% and 9%) [49]. Migrant blood/plasma donors were found to have higher HIV prevalence than nonmigrants in Hubei province [30].

Men Having Sex with Men (MSM)

One estimate suggests that there are up to 8 million MSM in China [47]. While homosexual activities are not illegal in China, neither are they socially acceptable. Gay or bisexual men are still under social pressure to hide their sexual orientation and to be mar-

ried [50, 51]. This often makes it very difficult to provide education to MSM about safer-sex practices and to conduct research. Married MSM may acquire HIV from their high-risk male sexual partners and transmit to their low-risk wives. A convenience sample of 481 homosexual men in Beijing showed 3.1% to be HIV positive, and 49% of participants reported unprotected anal intercourse in the previous 6 months [51]. A molecular epidemiologic study found a predominance of subtype B among Beijing MSM, suggesting an origin from the United States, Europe, Australia, or selected Asian cities [52].

Blood Recipients

Since 1995, China has developed strict guidelines to demand that all blood be screened for HIV and other blood-borne diseases before clinical use. However, there are still HIV cases reported through blood transfusion in rural areas. Several reasons exist for iatrogenic transmission, including a failure to screen blood and blood products, shortages and/or reuse of injection equipment, unnecessary injection or transfusion, ineffective sterilization of medical equipment, and lack of training in universal precautions.

Children Born to HIV-Infected Mothers

Although pregnant women and children have been at low risk to date, as the HIV epidemic spreads further, increasing numbers of low-risk women will be infected and mother-to-child transmission will increase. Sentinel HIV data in the higher prevalence Yunnan province showed little change among pregnant women, going from 0.15% in 1991-1998 to 0.2% in 1998-2001 [53-55], but it increased to 0.37% in 2003 (Chinese Ministry of Health/Chinese Center for Disease Control). The transmission rate was 38%

in one Chinese study, reflecting cumulative antenatal, intrapartum, and breastfeeding risk in the absence of antiretroviral intervention [33, 56]. Mother-to-child transmission is probably increasing where outbreaks have occurred among needle-sharing drug users and paid plasma/blood donors in the 1990s, but these transmission events may be underreported. Through 2002, only 96 cumulative perinatal cases had been reported nationwide, though 73 of these cases (76%) were reported in 2001 and 2002 [2].

FUTURE PERSPECTIVES

One should be cautious in predicting future trends for HIV/AIDS based on the past epidemic in China. Cumulative reported cases do not reflect recent incident HIV infections, but represent cumulative transmission patterns over the past two decades. For example, many plasma donors got infected in the 1990s but were reported with HIV or AIDS only recently. Furthermore, the average 30% rise in HIV/AIDS per year during 1998-2002 and the 54% rise in 2003, compared to 2002, may be due to improved screening and surveillance efforts, and may not reflect the precise magnitude of a rising trend.

IDU is the dominant transmission route in the recognized epidemic so far. The number of HIV infections among drug users will continue to rise given the increasing number of drug users and high levels of injection and needle sharing. The declining proportion of IDU cases in the cumulative reported cases, from 73% in 1994 to 64% in 2002, reflects more the expansion of HIV than any prevention successes among IDUs. Many IDUs are rural farmers who are less mobile, less financially affluent, and live in the relative remote areas of Yunnan, Xinjiang, or Guangxi provinces. If drug use itself expands, and especially if more urban residents become IDUs, the risk of transmitting HIV among

IDUs themselves and to the general population will increase without risk reduction and drug prevention/treatment intervention.

Commercial plasma donation activities are not now a major risk for new infections. However, infected former donors are developing clinical AIDS and represent a huge clinical care challenge. In Shanxi province, where FPDs account for 76% of all infections, AIDS case reports are rising much faster than HIV-non-AIDS cases, despite expanded voluntary counseling and testing in recent years [57]. Providing antiretroviral (ARV) therapy and care in these rural communities presents logistical, financial, and staffing challenges, China lacks trained physicians and nurses to provide ARV regimens and medical facilities to monitor ARV therapy, especially in rural communities hit hard by HIV. The historical "barefoot doctor" system is no longer a free service, nor are these now-upgraded allied health professionals yet qualified to provide ARV-based care.

Several factors may influence future HIV trends among MSM. Homosexual activity is not socially acceptable at present; many, if not most, Chinese would consider MSM an abnormality, more stigmatized than female commercial sex work. Recognized MSM tend to be more educated, live in large cities, and have a wide social network [50, 51], which potentially increases their likelihood of adopting HIV prevention methods through a peer education mechanism. On the other hand, the stigma of male homosexual activities drives MSM underground and hinders preventive and educational programs. Of 481 participants in Beijing, 49% reported unprotected anal intercourse with men, and 22% reported unprotected anal or vaginal intercourse with women in the past 6 months [51]. The wide social network of many urban MSM may put them at increasing risk as China continues its social and sexual liberalization. However, based on limited available data,

MSM are not likely to account for a large part of the total Chinese HIV/AIDS epidemic in the near future.

Heterosexual transmission is becoming a growing concern because of widespread commercial sex and the low rate of condom use in China. Thailand experienced "5 waves" of HIV/AIDS epidemic: from injection drug users, to female sex workers, to STD patients, to the wives and girlfriends of STD patients, and to their infants. Men who frequented CSWs were the key group bridging HIV transmission from the "core population" to the general population [58]. In China, sex workers and their male clients may become a similar bridge. Furthermore, some female sex workers are also drug users, often using CSW to support their drug habits [44, 59]. This sub-group, with both commercial sex and drug use risk, is of the highest public health importance.

Our review documents a growing HIV/AIDS epidemic in China. The window for China to forestall a generalized epidemic is narrowing. Interventions targeting at-risk sub-groups should be accompanied by mass media campaigns as a cost-effective way to increase the awareness of prevention among general population. Considering China's huge population size and wide geographic area, the extensive reach of the centralized Chinese media should be exploited. The central Chinese government has begun to take a pragmatic attitude towards HIV prevention and control efforts. Pilot projects of needle exchange and methadone maintenance treatment are being implemented; the China CARES Project was initiated in 2003 in 51 county-level communities with high proportions of former plasma donors or drug users. The China CARES Project provides HIV counseling and testing, ARV therapy and care, and prevention of mother-to-child transmission. However, many local government officials remain unconvinced; only with

commitment and support from both the central government and local governments is it possible to scale up interventions from their current pilot levels. We hope that this report can be updated in 2-3 years to describe the successes of Chinese efforts to reduce HIV transmission and expand HIV care and treatment.

REFERENCES

1. Joint United Nations Programme on HIV/AIDS (UNAIDS). National response brief – China. Available at: http://www.unaids.org/nationalresponse/result.asp (Accessed 18 March 2005).

2. Ministry of Health of China. National HIV/AIDS Case Report, 2003 (unpublished).

3. Zhao CZ, Liu ZM, Zhao D, et al. Drug abuse in China. Ann NY Acad Sci **2004;** 1025:439-45.

4. Beyrer C, Razak MH, Lisam K, et al. Overland heroin trafficking routes and HIV-1 spread in south and south-east Asia. AIDS **2000;** 14:75-83.

5. Kulsudjarit K. Drug problem in southeast and southwest Asia. Ann NY Acad Sci **2004**; 1025:446-57.

6. Ming ZQ, Liang SL, Yap L, et al. Qualitative study of drug using and sexual behaviors of drug users in Guangxi. Zhonghua Liu Xing Bing Xue Za Zhi **2002;** 23:111-3.

7. Ministry of Health of China. National HIV Sentinel Surveillance Reports, 1995-2003 (unpublished).

8. Ma Y, Li ZZ, Zhang KX, et al. HIV was first discovered among IDUs in China. Zhonghua Liu Xing Bing Xue Za Zhi **1990;** 11:184-5.

9. Zheng XW, Tian C, Choi KH, et al. Injecting drug use and HIV infection in southwest China. AIDS **1994;** 8:141-7.

10. Nelson KE. The epidemiology of HIV infection among injecting drug users and other risk populations in Thailand. AIDS **1994;** 8:1499-500.

11. Htoon MT, Lwin HH, San KO, et al. HIV/AIDS in Myanmar. AIDS **1994;** 8(Suppl 2):S105-9.

12. Piyasirisilp S, McCutchan FE, Carr JK, et al. A recent outbreak of human immunodeficiency virus type 1 infection in southern China was initiated by two highly homogeneous, geographically separated strains, circulating recombinant. J Virol **2000;** 74:11286-95.

13. Yu XF, Liu W, Chen J, et al. Rapid dissemination of a novel B/C recombinant HIV-1 among injection drug users in southern China. [letter]. AIDS **2001;** 15:523-538.

14. Qing GM, Shao YM, Liu G, et al. Genetic sequence and subtypes of HIV-1 in Sichuan Province. Zhonghua Liu Xing Bing Xue Za Zhi **1998;** 19:39-42.

15. Chen HH, Zhang JP, Kou JD, et al. The trend of HIV spread across the whole province of Yunnan – surveillance report of Yunnan 1995. Zhongguo Xing Bing Ai Zi Bing Fang Zhi **1996;** 2:54-7.

16. Chen HH, Zhang JP, Pan SF, et al. Analysis and prediction on the trends of HIV infection epidemic in Yunnan province. Zhongguo Xing Bing Ai Zi Bing Fang Zhi **2000;** 6:257-60.

17. Liu W, Chen J, Li ZJ, et al. Analysis of HIV epidemic trends in Guangxi, China. Guangxi Yu Fang Yi Xue **2001;** 7:257-9.

18. Lin P, Xu RH, Zeng CH, et al. The trend and characteristics of HIV/AIDS epidemic in Guangdong Province, 1986-1999. Zhonghua Liu Xing Bing Xue Za Zhi **2001;** 22:194-7.

19. Lin M, Lin P, Li H, et al. Epidemiological study on HIV/AIDS in Guangdong Province. Zhongguo Xing Bing Ai Zi Bing Fang Zhi **2001;** 7:11-3.

20. Ministry of Health (MOH), National Center for AIDS Prevention and Control (NCAIDS), and Collaboration Group for National HIV Sentinel Surveillance Program. Set up of national sentinel surveillance of HIV infection in China and its report in 1995. Zhongguo Xing Bing Ai Zi Bing Fang Zhi **1996;** 2:193-7.

21. Shan H, Wang JX, Ren FR, et al. Blood banking in China. Lancet **2002;** 360: 1770-5.

22. Wu ZY, Rou KM, Detels R. Prevalence of HIV infection among former commercial plasma donors in rural eastern China. Health Policy Plann **2001;** 16:41-6.

23. Beach MV. "Blood heads" and AIDS haunt China's countryside. Lancet **2001;** 357:49.

24. Wu ZY, Liu ZY, Detels R. HIV-1 infection in commercial plasma donors in China [letter]. Lancet **1995;** 346:61-2.

25. Zheng XW. Stop the spread of HIV among drug users and blood donors in China. Zhonghua Liu Xing Bing Xue Za Zhi **2000;** 21:6.

26. Wang Ying. China shuts down illegal blood stations. China Daily October 21, 2004. Available at: http://www.chinadaily.cn/english/doc/2004-10/21/content_384165.htm (Accessed 10 May 2005).

27. Su HC. Blood-borne diseases in plasma samples in Henan Province. Ji Bing Jian Ce **1997;** 12:251-3.

28. Yan JY, Zheng XW, Zhang XF, et al. The survey of prevalence of HIV infection among paid blood donors in one county of China. Zhonghua Liu Xing Bing Xue Za Zhi **2000;** 21:10-2.

29. Liu SZ, Zheng XW, Fu JH, et al. HIV prevalence and subtypes among paid blood donors in Shandong and Hubei provinces, China. Zhongguo Yu Fang Yi Xue Za Zhi **2001;** 2:8-11.

30. Liu ZF, Mei ZQ, Zheng XW, et al. Investigation of HIV infection among plasma donors in three illegal plasma collection places in central China. Zhonghua Liu Xing Bing Xue Za Zhi **2000;** 21:466-7.

31. Liu SZ, Fu JH, Su SL, et al. Survey of HIV infection among blood donors in a rural area in Shangdong Province. Shi Yong Yu Fang Yi Xue **2000;** 7:430-1.

32. Chen X, He JM, Wu HQ, et al. A seroepidemiolgic and behavioral study of HIV, HCV, HBV and syphilis infection among commercial blood donors. Shi Yong Yu Fan Yi Xue **1999;** 6:174-6.

33. Zhuang K, Gui XE, Su B, et al. High prevalence of HIV infection among women and their children in Henan Province, China [letter]. J Acquir Immune Defic Syndr **2003;** 33:649-57.

34. Zheng XW, Wang Z, Xu J, et al. The epidemiological study of HIV infection among paid blood donors in one county of China. Zhonghua Liu Xing Bing Xue Za Zhi **2000;** 21:253-5.

35. Chen H, Qian X, Cao GH, et al. Study on the seropositive prevalence of human immunodeficiency virus in a village residents living in rural region of central China. Zhonghua Liu Xing Bing Xue Za Zhi **2004;** 25:317-21.

36. Chu W, Huang CH. Gonorrhea among prostitutes: a survey of the incidence and an attempt at oral sulfadiazine prophylaxis. Chung Hua I Hsue Tsa Chih **1948;** 66:312-18.

37. Cohen MS, Henderson GE, Aiello P. Successful eradication of sexually transmitted diseases in the People's Republic of China: Implications for the 21st century. J Infect Dis **1996;** 174(Suppl):S223-9.

38. Liao SS, Schensul J, Wolffers I. Sex-related health risks and implications for interventions with hospitality women in Hainan, China. AIDS Educ Prev **2003;** 15:109-21.

39. Huang YY, Henderson GE, Pan SM, et al. HIV/AIDS risk among brother-based female sex workers in China: assessing the terms, content, and knowledge of sex worker. Sex Transm Dis **2004;** 31:695-700.

40. Pan SM, Parish WL, Wang AL, eds. [Zhongguoren de Xing Guangxi yu Xing Xingwei 1999-2000 (Chinese People's Sexual Relationships and Sexual Behavior)]. Beijing: Social Science Document Publishing House; 2004.

41. World Health Organization Western Pacific Region. Sex Work in Asia. **2001.** Available at: http://www.wpro.who.int/siteserver/knowledge/search/SearchRight.asp?ct=ALL&q1=sex+work+in+Asia (Accessed 18 March 2005).

42. Pan SM, ed. Cun Zai Yu Huang Miu—Zhong Guo Di Xia Xing Chan Ye Kao Cha. Beijing: Qunyan Publishing House; 2001.

43. Gil VE, Wang MS, Anderson AF, et al. Prostitutes, prostitution and STD/HIV transmission in mainland China. Soc Sci Med **1996;** 42:141-52.

44. Qian HZ, Zhao PF, Jiang YF, et al. Demographic profile and HIV risk behaviors among female drug users in Shanghai [Abstract 23576]. Presented at 12th World AIDS Conference; 1998; Geneva.

45. Zhang JY. The past, present and future epidemic of sexually transmitted diseases in China. Zhonghua Liu Xing Bing Xue Za Zhi **1998;** 19:118-21.

46. Gong XD, Ye SZ, Zhang GC, et al. An epidemiological analysis of sexually transmitted diseases in China in 2000. Zhongguo Xing Bing Ai Zi Bing Fang Zhi **2001;** 7:131-4.

47. Zhang KL, Ma SJ. Epidemiology of HIV in China [Editorial]. BMJ **2002;** 324:803-4.

48. Liao SS. HIV in China: epidemiology and risk factors. AIDS **1998;** 12(Suppl):S19-25.

49. Anderson AF, Qingsi Z, Hua X, et al. China's floating population and the potential for HIV transmission: a social-behavioral perspective. AIDS Care **2003;** 15:177-95.

50. Zhang BC, Liu DC, Li XF, et al. A survey of men who have sex with men: mainland China [letter]. Am J Public Health **2000;** 90:1949-50.

51. Choi KH, Liu H, Guo YQ, et al. Emerging HIV-1 epidemic in China in men who have sex with men [letter]. Lancet **2003;** 361:2125-6.

52. Yao J, Zhang FJ, He ZP, et al. Subtypes of HIV infection among homosexuals in Beijing. Zhonghua Liu Xing Bing Xue Za Zhi **2003;** 24:159.

53. Li H, Mo LH, Liu H, et al. Prevention of HIV transmission from mother to child in Yunnan. Xian Dai Yu Fang Yi Xue **2001;** 28:68-9.

54. Zhang XB, Ma YL, Yu HF, et al. Analysis of HIV/AIDS surveillance data in Yunnan, 2001. Ji Bing Jian Ce **2002;** 17:327-9.

55. Yuan JH, Ionita G, Xu Y, et al. The HIV/AIDS projection in Yunnan. Zhongguo Xing Bing Ai Zi Bing Fang Zhi **2002;** 8:78-81.

56. Cao YZ, Li GH, Wang SY, et al. Current situation, crisis and control strategies of HIV-1 mother-to-child transmission in China. Zhongguo Chuan Ran Bing Xue Za Zhi **2002;** 20:185-8.

57. Qiao XC, Nie XY, Guo XL. Analysis of the epidemic of HIV/AIDS in Shanxi province and the strategy for HIV/AIDS prevention and control. Zhongguo Xing Bing Ai Zi Bing Fang Zhi **2004;** 10:190-2.

58. Morris M, Podhisita C, Wawer MJ, et al. Bridge populations in the spread of HIV/AIDS in Thailand. AIDS **1996;** 10:1265-71.

59. Zhao PF, Yu H. Study on sexual and drug use behaviors of high risk among sex workers in entertainment establishments in Shanghai. Zhonghua Liu Xing Bing Xue Za Zhi **2001;** 22:341-3.

BETTER KNOWLEDGE PREDICTS FEWER DISCRIMINATORY ATTITUDES TOWARD HIV/AIDS IN RURAL COMMUNITIES WITH FORMER COMMERCIAL PLASMA DONORS IN CHINA

by

HANZHU QIAN, XIAOMING SHI, ERIC CHAMOT, HUEY CHEN, JIANGHUA GAO, ZHONGMIN YANG, STEN H. VERMUND, YIMING SHAO, AND NING WANG

In preparation for *AIDS PATIENT CARE and STDs*

Format adapted for dissertation

ABSTRACT

Little is known about HIV/AIDS related knowledge and attitudes in rural communities with former plasma donors and HIV/AIDS cases in rural China. We conducted a survey of 524 randomly selected adult villagers in Shanxi Province to test a hypothesis that better knowledge is associated with less discrimination. Most villagers knew that HIV can be transmitted by sex (95% correct answer), blood transfusion (97%) and needle sharing (93%), and during pregnancy (88%), delivery (74%), and breast feeding (75%), whereas 84% also knew that condom use is protective. Many believed that HIV infection can be acquired by mosquito bites (70%), swimming (42%), sharing meals (26%), shaking hands (24%), and speaking face to face (24%). Discriminatory attitudes were frequent: high proportions of villagers reported they would keep away from infected individuals (50%) and their family members (36%), and be reluctant to buy fresh vegetables from stall-keepers with AIDS (79%), to allow their children to play with an infected child (82%), or to allow a teacher with HIV to teach in school (57%). Discriminatory attitudes were significantly associated with low knowledge and education, older age, and married status in a logistic regression analysis. Our survey suggests that community education to eliminate misconceptions and increase knowledge may help reduce HIV/AIDS stigma and discrimination.

INTRODUCTION

Stigma related to acquired immunodeficiency syndrome (AIDS) has been defined as "the prejudice, discounting, discrediting, and discrimination that are directed at people

perceived to have AIDS" [1]. Stigma and discrimination against people living with human immunodeficiency virus (HIV)/AIDS have existed worldwide since the start of the epidemic [2,3], and have imposed double jeopardy on the lives of people who are living and struggling with the disease [4-7]. people living with HIV/AIDS were driven from their homes and subjected to social abuse [4,5], and they received unequal treatments in employment and health care [6]. As the results, discrimination deterred them from obtaining HIV testing, disclosing their seropositive status to sexual partners, family, and friends, and accessing to antiretroviral therapy and other cares [7-9].

It is generally believed that the reasons of stigma and discrimination are complex. Stigma is deeply rooted in the convoluted domains of gender, race, ethnicity, class, sexuality, and culture [10]. However, misunderstanding about the mechanisms of HIV/AIDS transmission and perceptions of the "immorality" of behaviors related to HIV/AIDS infection are two frequently reported causes. Gay men and injection drug users have been discriminated because they are disproportionately affected by the epidemic and because they have "immoral" sexual orientation or drug using behavior [11,12]. Overestimation of the risk of contracting HIV via casual social contact has been found to be associated with discrimination [13,14].

Illegal plasma collection practices were popular in some rural areas in central-eastern China in 1990s. These practices with pooling blood samples and reinfusing erythrocytes to the donors caused a large number of HIV infections [15]. However, very few studies have investigated HIV/AIDS related knowledge and attitudes in these affected rural communities [16], which are important for developing intervention projects. In this study, we examined HIV/AIDS knowledge and attitudes in rural villages in Shanxi Prov-

ince in central China, where illegal commercial plasma collection practices in the mid-1990s caused HIV/AIDS infections among donors. We tested a hypothesis that better HIV/AIDS knowledge is associated with fewer discriminatory attitudes towards persons with HIV/AIDS. We also made comparisons for sex and plasma/blood donation regarding HIV/AIDS knowledge and attitudes.

METHODS

Sampling and Data Collection

As a part of a larger ongoing project — China Integrated Programs for Research on AIDS, this cross-sectional epidemiologic survey was conducted in November and December 2003 in 12 villages with former plasma/blood donors (FPDs) in rural Shanxi Province in central China. A total of 660 villagers aged 18-59 years were randomly selected from a sampling framework of 9205 villagers. Eligibility criteria were as follows: permanent residents in the targeted villages, age 18-59 years old, able and willing to provide informed consent, and able and willing to provide contact information.

Written informed consent was obtained from each participant before collecting any data. Standardized questionnaire interviews were administered by same-sex, trained interviewers who collected demographic and medical histories; behavioral data, including blood donation history; and knowledge, attitudes, and behavioral data. Questionnaire completion was monitored by internal and external quality controls. The study protocol was approved by the institutional review board of the Chinese National Center for AIDS/STD Prevention and Control and the University of Alabama at Birmingham, as well as by the National Institute of Allergy and Infectious Diseases.

Measures

HIV/AIDS knowledge was assessed by 19 items covering modes of transmission, prevention, clinical outcomes, and treatments. These questions were adapted from the Family Health International HIV/AIDS/STD Behavioral Surveillance Surveys (FHI BSS) [17], and the World Health Organization (WHO) Research Package: Knowledge, Attitudes, Beliefs and Practices on AIDS [18]. Answers to knowledge questions were coded as yes/no/don't know/no response; we assigned a score of 1 to the correct answer and 0 to all other answers. A summary variable was obtained for each participant by adding up the scores from 19 knowledge items.

Five attitude questions were developed by adapting FHI BSS questions to local realities: "If a teacher has the HIV/AIDS virus, but is not sick, should he or she be allowed to continue teaching in school?" "Would you buy fresh vegetables from a stall-keeper with AIDS?" "Would you allow your child to play with a child who has HIV/AIDS?" "If you knew one of your neighbors was infected with AIDS virus, how would you treat him/her?" "If you knew one of your neighbors was infected with AIDS virus, how would you treat his or her family members?" These questions were pilot tested among local villagers and health care staff for clearness of expression and suitability before used in the study. Discriminatory attitudes were defined as an answer of "no" for the first 3 questions, and "keep away from the persons" for the last 2 questions. We assigned a score of 1 to the discriminatory answer and 0 to all other answers; the arithmetic sum of answers provided by each participant gave a summary variable with a value ranging from 0 to 5.

Demographic variables included sex, date of birth, ethnicity, marital status, occupation, education, and self-perception of economic status comparing with neighbors. Sexual and HIV-related behaviors included migration in the past 5 years, number of lifetime sexual partners, having ever had a commercial sex partner, having ever had a casual partner, having ever used condoms, and having ever used illicit drugs. Each participant was also asked whether they knew a person who was infected with HIV or had died of AIDS.

Statistical Analysis

Comparisons were first made for all socio-demographic variables and individual knowledge and attitude items between male and female participants, as well as between FPDs and nondonors. Kruskal-Wallis tests were used for comparing the means of age, and the knowledge and attitude scores. χ^2 tests were used for comparing categorical variables. We treated the attitude score as a continuous variable; its distribution was tested and found to be close to normal. A multiple linear regression model was fitted to estimate the factors associated with discriminatory attitudes, including the knowledge score as one of explanatory variables. A cumulative logit model, a more robust model for ordinal dependent variables [19], was also fitted by including the same variables in the linear regression model. Those variables not significant in the multiple linear regression and cumulative logit models at a significant level of $P < 0.05$ were eliminated in a backward manner, identifying variables that were independently associated with the attitude score. All analyses were performed by using SAS Software Version 9.0 (SAS Institute Inc., Cary, NC). All probability values were reported as 2-sided.

RESULTS

Demographic and Behavioral Characteristics

Five hundred forty villagers participated in the study. Of 120 nonparticipants, 81 left villages for temporary jobs in cities, 35 refused, and 4 died or were ineligible. Nonparticipants (58% males) had a similar sex distribution as participants (50% males), but nonparticipants (49% less than 30 years old) were younger than participants (20%)

Of 540 participants, 524 (97.0%) had ever heard of AIDS and therefore were included in the analyses for this paper. Among these 524 participants, 50.2% were males; 76.1% had attended middle school or above; 96% were married; all participants were Han majority ethnic Chinese; and 68.7% had other income in addition to farming. The mean age was 40.1 ± 11.0 years old. On average, males had higher levels of education and reported lower incomes than females. Marriage rates were high. FPDs were older than nondonors; they reported lower level of education and income than nondonors (table 1). The most common risk factor for HIV was former plasma/blood donation: 22.0% had a history of selling plasma or blood; 11.8% had more than one lifetime sexual partners; 6.5% villagers had commercial or casual sexual partners; 19.3% of villagers ever used condoms; 0.4% ever used illicit drugs; and 31.1% had ever left village for temporary jobs in the past 5 years.

Table 1. Sociodemographic characteristics of 524 adult residents who have heard of AIDS in rural Shanxi Provnce, China (2003).

	Total (*N*=524) *n* (column %)	Male (*N*=263) *n* (column %)	Female (*N*=261) *n* (column %)	*P*-value	FPDs (*N*=115) *n* (column %)	Non-FPDs (*N*=409) *n* (column %)	*P*- value
Age (years)							
mean ± SD	40.1 ± 11.0	40.0 ± 11.1	40.3 ± 11.0	0.73	45.5 ± 6.9	38.6 ± 10.7	<0.001
Education							
Elementary or lower	125 (23.9)	46 (17.5)	79 (30.3)	<0.001	46 (40.0)	79 (19.3)	<0.001
Middle or higher	399 (76.1)	217 (82.5)	182 (69.7)		69 (60.0)	330 (80.7)	
Marriage							
Single	21 (4.0)	14 (5.3)	7 (2.7)	0.12	0 (0.0)	21 (5.1)	0.013
Married	503 (96.0)	249 (96.7)	254 (97.3)		115 (100.0)	388 (94.9)	
Occupation (all were farmers)							
Having no other incomes	164 (31.3)	59 (22.4)	105 (40.2)	<0.001	37 (32.2)	127 (31.0)	0.82
Having other incomes	360 (68.7)	204 (77.6)	156 (59.8)		78 (67.8)	282 (69.0)	
Self-assessment on economic status comparing with neighbors							
Middle level or above	385 (73.5)	180 (68.4)	205 (78.8)	0.007	76 (66.1)	309 (75.5)	0.04
Lower than middle level	138 (26.5)	83 (31.6)	55 (21.2)		39 (33.9)	99 (24.3)	
Sex							
Male	263 (50.2)				59 (51.3)	204 (49.9)	0.79
Female	261 ((48.8)				56 ((48.7)	205 (50.1)	

Table 1. (Continued)

	Total (*N*=524) *n* (column %)	Male (*N*=263) *n* (column %)	Female (*N*=261) *n* (column %)	*P*- value	FPDs (*N*=115) *n* (column %)	Non-FPDs (*N*=409) *n* (column %)	*P*- value
Source of HIV/AIDS knowledge							
Friends or neighbors	332 (63.4)	140 (53.2)	192 (73.6)	<0.001	85 (73.9)	247 (60.4)	0.008
Television	299 (57.1)	157 (59.7)	142 (54.4)	0.22	59 (51.3)	240 (58.7)	0.16
Magazine & newspaper	100 (19.1)	64 (24.3)	36 (13.8)	0.002	11 (9.6)	89 (21.8)	0.003
Family members	32 (6.1)	7 (2.7)	25 (9.6)	<0.001	6 (5.2)	26 (6.4)	0.65
Radio	27 (5.2)	22 (8.4)	5 (1.9)	<0.001	4 (3.5)	23 (5.6)	0.36
Medical staff	23 (4.4)	15 (5.7)	8 (3.1)	0.14	5 (4.4)	18 (4.4)	0.98
School and teacher	11 (2.1)	4 (1.5)	7 (2.7)	0.35	0 (0.0)	11 (2.7)	0.08
Others	56 (10.7)	36 (13.7)	20 (7.7)	0.02	10 (8.7)	46 (11.2)	0.43

HIV/AIDS Knowledge

The most common sources for obtaining HIV/AIDS information were friends or neighbors (63.4%), and television (57.1%). In bivariate analyses, men were more likely than women to obtain knowledge from the radio, magazines, or newspapers, and less likely to seek knowledge from family members, friends, or neighbors. FPDs were more likely to obtain knowledge from friends or neighbors, and less likely to obtain information from magazines or newspapers, than nondonors. There were no sex differences in obtaining knowledge from television, medical staff, and school or teachers, or between FPDs and nondonors (table 1).

A high proportion of participants knew that a person could get HIV from sexual intercourse (94.8%), and that risk could be reduced by being abstinent from sex (91%), being faithful (93.1%) and using condoms (83.6%). Over 90% of villagers knew that a person could get HIV from receiving contaminated blood (96.8%) and sharing needles (93.1%). Most participants also knew that an infant could get HIV from an infected mother during pregnancy (87.6%), delivery (73.9%), and breast feeding (74.6%) (table 2). However, misconceptions about HIV included believing transmission to be possible by shaking hands (24.6%), sharing meals (26.5%), and speaking face to face (24%) with an infected person; 41.8% believed that swimming with an infected person and 70.4% that mosquito bites could transmit HIV. Nearly 57% participants said that avoiding drinking unboiled water can reduce the risk of HIV infection. Only 16.6% of participants knew that a healthy-looking person could be infected with HIV; 35.3% believed that AIDS could be cured.

Table 2. Knowledge about HIV/AIDS among 524 adult residents who have heard of AIDS in rural Shanxi Province, China (2003).

Items	Correct answer	Proportion of correct answers (%)						
		Total (*N*=524)	Male (*N*=263)	Female (*N*=261)	*P*- value	FPDs (*N*=115)	Non-FPDs (*N*=409)	*P*- value
Can a person get HIV from…?								
Shaking hands	No	75.4	78.7	72.0	0.08	67.8	77.5	0.03
Sharing a meal	No	73.5	76.4	70.5	0.12	64.3	76.0	0.012
Speaking face to face	No	76.0	79.5	72.4	0.06	63.5	79.5	<0.001
Swimming	No	58.2	61.6	54.8	0.11	54.8	59.2	0.40
Mosquito bite	No	29.6	28.1	31.0	0.47	27.8	30.1	0.64
Can a person get HIV from…								
Sexual intercourse	Yes	94.8	96.6	93.1	0.07	94.8	94.9	0.98
Blood transfusion	Yes	96.8	97.3	96.2	0.49	98.3	96.3	0.30
Sharing a needle	Yes	93.1	93.5	92.7	0.71	88.7	94.4	0.03
Sharing a shaver	Yes	62.4	64.6	60.1	0.29	63.5	62.1	0.79
Can an infant get HIV from his/her infected mother…?								
During pregnancy	Yes	87.6	86.3	88.9	0.37	84.4	88.5	0.23
During delivery	Yes	73.9	71.1	76.6	0.15	70.4	74.8	0.34
During breast feeding	Yes	74.6	71.9	77.4	0.14	71.3	75.6	0.97

Table 2. (continued)

Items	Correct answer	Proportion of correct answers (%)						
		Total (*N*=524)	Male (*N*=263)	Female (*N*=261)	*P*-value	FPDs (*N*=115)	Non-FPDs (*N*=409)	*P*- value
Can a person reduce the risk of contracting HIV by…?								
Abstinence	Yes	91.0	89.4	92.7	0.18	91.3	91.0	0.91
Being faithful	Yes	93.1	93.2	93.1	0.98	94.8	92.7	0.43
Using condom	Yes	83.6	85.9	81.2	0.15	81.7	84.1	0.54
Not drinking un-boiled water	No	56.9	54.0	59.0	0.25	53.0	57.5	0.40
Is there a vaccine available now to prevent HIV?	No	55.6	55.9	53.3	0.54	40.0	58.7	0.000
Can a person who has HIV/AIDS be cured?	Yes	16.6	19.0	14.2	0.19	19.1	15.9	0.41
Do you think a healthy-looking person can be infected with HIV?	No	35.3	22.1	48.7	0.000	44.4	32.8	0.02

Overall, participants correctly answered 14 (25%-75% interval: 12-16) out of 19 knowledge questions. More FPDs had misconceptions than nondonors about HIV transmission (e.g., shaking hands, sharing meals, and speaking face to face); fewer FPDs knew that sharing needles could transmit HIV (table 2). However, there is no statistically significant difference in knowledge scores for FPDs and nondonors. Men and women had similar knowledge (figure 1).

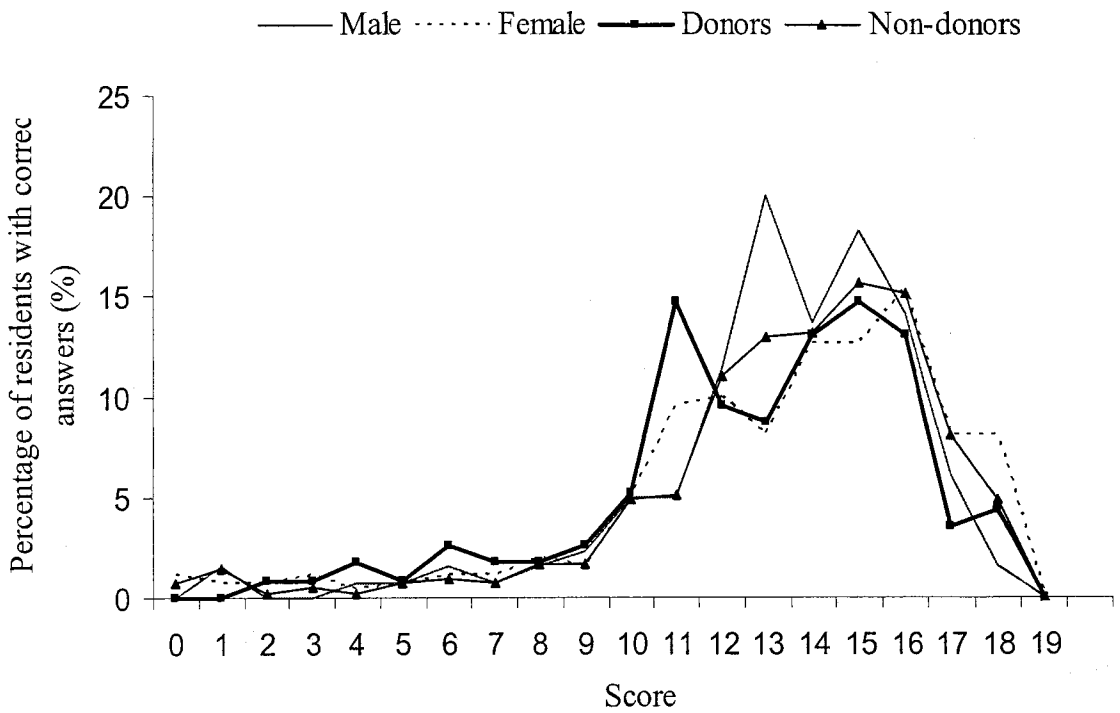

Figure 1. Range of correct answers to questions on HIV/AIDS knowledge among 524 adult residents in rural Shanxi Province, China (2003). Males vs. females $P = 0.92$; donors vs. nondonors $P = 0.06$.

Attitudes toward Persons with HIV/AIDS

Discriminatory attitudes are very common in these communities. About 80% participants reported that they would not buy fresh vegetables from a stall-keeper with AIDS

and would not allow their children to play with a child with HIV/AIDS. Over half said that they would not allow a teacher with HIV to continue teaching in school, and they would keep away from a neighbor with HIV. About one third of participants said that they would keep away from family members of an HIV-infected person. Men and women had similar attitudes; FPDs were more likely to have discriminatory attitudes than nondonors (table 3). When asked "Who is responsible for providing the daily care of AIDS patient?" 72.5% participants reported family members and 17.0% reported health care organizations.

Nine predictor variables that were significant in univariate analyses or may potentially influence attitudes toward HIV/AIDS were entered into multiple linear regression and cumulative logit models, including demographic variables (sex, age, education, marital status, occupation, and self perception of economic status), whether the respondent had a history of selling plasma or blood, whether the respondent knew a person with HIV/AIDS, and knowledge score. Knowledge score, age, and marital status were independently associated with attitude score in a linear regression model. Every 1-unit increase in knowledge score was associated with a 0.12-unit decrease in discriminatory attitude score; older villagers have more discriminatory attitudes than younger ones; married villagers have more discriminatory attitudes than unmarried ones. Besides these 3 independent variables in linear regression model, education was also independently associated with attitude score in cumulative logit model. The cumulative logit model predicted more versus fewer discriminatory attitudes with a coded value from 5 to 0. Participants with higher knowledge score had fewer discriminatory attitudes than those with lower

Table 3. Discriminatory attitudes regarding HIV/AIDS among 524 adult residents who have heard of AIDS in rural Shanxi Province, China (2003).

Items	Discriminatory attitude	Proportion of answers (%)						
		Total (*N*=524)	Male (*N*=263)	Female (*N*=261)	*P*-value	FPDs (*N*=115)	Non-FPDs (*N*=409)	*P*-value
If a teacher has the HIV/AIDS virus, but is not sick, should he or she be allowed to continue teaching in school?	No	57.2	58.2	55.9	0.61	67.0	54.3	0.015
Would you buy fresh vegetables from stall-keeper with AIDS?	No	79.0	77.2	80.8	0.30	90.4	75.6	<0.001
Would you allow your child to play with a child who has the HIV/AIDS?	No	81.9	80.6	83.1	0.45	91.3	79.2	0.001
If you knew one of your neighbors was infected with AIDS virus, how would you treat him/her?	Avoid	50.0	46.0	54.0	0.07	60.0	47.2	0.015
If you knew one of your neighbors was infected with AIDS virus, how would you treat his or her family members?	Avoid	35.9	31.2	40.6	0.02	43.5	33.7	0.054

NOTE. Avoid=respondents say that they will keep away from the person.

knowledge score (cumulative logit model odds ratio = 0.87 < 1); villagers who had attended middle or higher schools had fewer discriminatory attitudes than those who had attended elementary school or had no education. Sex, occupation, self-perception of economic status, having a history of selling plasma or blood, and knowing a person with HIV/AIDS were not associated with attitudes (table 4).

Table 4. Factors associated with discriminatory attitudes against persons with HIV/AIDS among 524 adult residents who have heard of AIDS in rural Shanxi Province, China (2003).

Factors	Linear regression model		Cumulative logit model *	
	B	*P*-value	OR (95% CI)**	*P*-value
Knowledge score	-0.12	<0.001	0.87 (0.82-0.91) †	<0.001
Age	0.03	<0.001	1.03 (1.02-1.05) ‡	<0.001
Marital status	0.82	0.02		0.03
Single			1.0	
Married			2.51 (1.18-5.81)	
Education	–	–		0.02
Elementary or lower			1.0	
Middle or higher			0.64 (0.43-0.94)	

NOTE. * Predicting higher versus lower level of discrimination. ** OR: odds ratio; CI: confidence interval. † Every 5-point increase in knowledge score. ‡ Every 5-year increase in age.

DISCUSSIONS

The results of this study confirmed our *a priori* hypothesis that discriminatory attitudes toward HIV/AIDS were independently associated with lower HIV-related knowledge in rural communities with former plasma donors and HIV/AIDS. Discriminatory attitudes were also significantly associated with older age, married status, and lower education. In general, residents in these rural communities had a fairly good base of HIV knowledge; over 93% of villagers knew that HIV can be transmitted via sexual inter-

course, blood transfusion, or sharing a needle; about three quarters of villagers knew that HIV can be transmitted from mothers to infants during pregnancy, delivery, or breast feeding. However, misconceptions about HIV nontransmission routes and clinical outcomes were common, e.g., HIV transmission via mosquito bites or by swimming. Discriminatory attitudes toward HIV/AIDS were highly prevalent. This same pattern of good knowledge about HIV transmission routes, but coexisting misconceptions and discriminatory attitudes was seen in a national survey in 2004; for example, 90% of surveyed urban and rural residents knew that HIV/AIDS was an infectious disease; 67% said mosquito bites could transmit HIV; only half agreed that individuals with HIV/AIDS had same right as others to attend school or to work [20].

HIV/AIDS cases have been reported since the late 1990s in the study communities and local hospitals, and disease control departments have conducted a few education programs. These education programs typically emphasize the principal modes of HIV transmission, but fail to provide comprehensive information and stigma reduction education. That may explain the mixed status of good knowledge on transmission routes, but misconceptions on nontransmission routes. Misconceptions about nontransmission routes may heighten fears of HIV/AIDS and explain common discriminatory attitudes.

Discriminatory attitudes do not necessarily result in blatant discriminatory actions, such as violence against people with HIV/AIDS; as in the Chinese culture generally, people would be reluctant to do something openly and make others "lose face." However, residents in rural China are often socially connected; they know all of their neighbors in the village and even in other nearby villages, they work together, and they dine together in wedding parties or funeral ceremonies. This close social connection may increase the

possibility of adverse impacts on infected people and in communities of HIV-associated stigma and discrimination. Stigma remains a major obstacle to mounting an effective response to the epidemic [8,9]. FPDs may not be willing to take an HIV test as they are afraid of knowing a positive result; therefore, infected but undetected villagers may continue to transmit HIV to their spouses and/or other sexual partners through sexual contact or to their children through the mother-to-child route. The iatrogenic route of transmission is a continuing concern because while illegal blood donation practices have been curtailed, universal precautions are still not taken in medical practices in rural China. As more and more infected FPDs begin to develop AIDS, their illnesses will become apparent and are more likely to have discrimination problems.

The knowledge of AIDS was negatively correlated with AIDS social anxiety and desire for restrictions on patient civil liberties in a United States study [13]. A belief among Botswanan young people of getting an HIV infection by sharing a meal with an HIV/AIDS patient was associated with discriminatory attitudes towards persons living with HIV/AIDS [14]. Our study findings support the conclusion that there is a negative association between HIV knowledge and discrimination, and they suggest that intervention projects should emphasize on eliminating misconceptions and increasing knowledge, and therefore reducing stigma and discrimination, especially for married and older villagers and those with lower education.

Family value has a central role in Chinese culture. It has been a long tradition in China that family members support each other to achieve success as well as to confront difficulties and disasters. Our study showed that more than 70% of villagers believed that family members should be responsible for taking daily care of an HIV/AIDS patient.

Thus far, a majority of HIV/AIDS cases in China have been reported in rural areas. Rural residents often lack health insurance and cannot afford health care expenditures. Though the Chinese government has begun to provide free antiretroviral drugs to infected rural residents, hospitalization costs are not covered. Thus, the only practical option for most AIDS patients in rural areas is to stay at home and be taken care of by family members. Intervention programs should involve family members of HIV/AIDS patients, educating them about medication use, nutrition, and transmission prevention to increase their care-giving capabilities.

Our community-based study had several strengths. We conducted a community census from which a random sample was drawn. Voluntary participation, confidential interview, and strict quality control increased the validity of the data. The study also had limitations. Nonparticipation in our study might affect our estimation of the prevalence of HIV/AIDS knowledge and attitudes. Nonparticipants were younger than participants; most of them left villages seasonally for temporary jobs. They might be more exposed to HIV/AIDS educational information, i.e., their misconceptions and discriminatory attitudes might be lower than participants. But nonparticipation is not likely to imperil our *a prior* hypothesis testing of the relationship between knowledge and attitude.

CONCLUSION

Residents in rural Chinese communities with former plasma donors and HIV/AIDS cases had high levels of knowledge on HIV transmission routes, but they had misconceptions about HIV nontransmission routes and discriminatory attitudes toward people with HIV/AIDS. Persons with lower knowledge, lower educational levels, were

older, or were married had more discriminatory attitudes. As more and more former plasma donors who were infected in early 1990s develop AIDS, stigma and discrimination issues will become more apparent and should be urgently addressed.

REFERENCES

1. Corrigan PW, Penn DL. Lessons from social psychology on discrediting psychiatric stigma. Am Psychol **1999;** 54:765-76.

2. Herek GM, Glunt EK. An epidemic of stigma: public reactions to AIDS. Am Psycho **1988;** 43:886-91.

3. Blendon RJ, Donelan K. Discrimination against people with AIDS: the public perspective. N Engl J Med **1988;** 319:1022-6.

4. Zierler S, Sunningham WE, Andersen R, et al. Violence victimization after HIV infection in a US probability sample of adult patients in primary care. Am J Public Health **2000;** 90:208-15.

5. Gielen AC, O'Campo P, Faden RR, et al. Women's disclosure of HIV status: experiences of mistreatment and violence in an urban setting. Women Health **1997;** 25:19-31.

6. Gostin LO, Webber D. The AIDS litigation project: HIV/AIDS in the courts in the 1990s, part 2. AIDS Public Policy J **1998;** 13:3-19.

7. Kalichman SC, Simbayi LC. HIV testing attitudes, AIDS stigma, and voluntary HIV counseling and testing in a black township in Cape Town, South Africa. Sex Transm Infect **2003;** 79:442-7.

8. Ford K, Wirawan DN, Sumantera GM, et al. Voluntary HIV Testing, Disclosure, and Stigma Among Injection Drug Users in Bali, Indonesia. AIDS Educ Prev **2004;** 16:487-98.

9. Carr RL, Gramling LF. Stigma: a health barrier for women with HIV/AIDS. J Assoc Nurses AIDS Care **2004;** 15:30-9.

10. Valdiserri RO. HIV/AIDS stigma: an impediment to public health. Am J Public Health **2002;** 92:341-2.

11. Diaz RM. Ayala G, Bein E. Sexual risk as an outcome of social oppression: data from a probability sample of Latino gay men in three U.S. cities. Cultur Divers Ethnic Minor Psychol **2004;** 10:255-67.

12. Day C, Ross J, Dolan K. Hepatitis C-related discrimination among heroin users in Sydney: drug user or hepatitis C discrimination? Drug Alcohol Rev **2003;** 22:317-21.

13. Bean J, Keller L, Newburg C, et al., Methods for the reduction of AIDS social anxiety and social stigma. AIDS Educ Prev **1989;** 1:94-221.

14. Letamo G. Prevalence of, and factors associated with, HIV/AIDS-related stigma and discriminatory attitudes in Botswana. J Health Popul Nutr **2003;** 21:347-57.

15. Zheng XW. Stop the spread of HIV among drug users and blood donors in China. Zhonghua Liu Xing Bing Xue Za Zhi **2000;** 21:6.

16. Wang L, Huang QQ, Xu J, et al. KAP survey among blood donors in Yiwu City, Zhejiang Province in 1997. Zhongguo Xingbing Aizibing Za Zhi **1999;** 5:18-20.

17. Family Health International. FHI 2000 HIV/AIDS/STD Behavioral Surveillance Surveys (BBS). Available at: www.who.int/hiv/strategic/bbs_fhi2000.pdf (Accessed 18 March 2005).

18. World Health Organization. Research Package: Knowledge, Attitudes, Beliefs and Practices on AIDS (KABP) Phase 1. WHO, Geneva. **1990.**

19. Allison PD. Logistic Regression Using the SAS. Cary, NC: SAS Institute. **1999.**

20. Ministry of Health of China. AIDS KAB Study among Chinese Residents in 2004 (unpublished).

HEPATITIS C VIRUS IN COMMUNITIES WITH FORMER COMMERCIAL PLASMA DONORS IN RURAL SHANXI PROVINCE, CHINA: THE CHINA-CIPRA PROJECT

by

HANZHU QIAN, ZHONGMIN YANG, XIAOMING SHI, JIANGHUA GAO, CUILIN XU, LAN WANG, KAI ZHOU, YAN CUI, XIWEN ZHENG, ZUNYOU WU, FAN LU, SHENGHAN LAI, STEN H. VERMUND, YIMING SHAO, AND NING WANG

Submitted to *The Journal of Infectious Diseases*

Format adapted for dissertation

ABSTRACT

Illegal plasma donation in the late 1980s and early 1990s spread blood-borne infections in central China. A cross-sectional survey was conducted in 2003 among a random sample of 538 adult residents from 12 former commercial plasma donating villages in rural Shanxi Province. Structured questionnaires were administered and blood samples were tested for HCV antibodies. HCV seroprevalence rates were 8.2% in all participants, 27.7% in donors, and 2.6% in nondonors. Selling blood or plasma was the strongest independent predictor for HCV seropositivity (OR=14.4; 95% CI: 7.1-31.6). Receiving a blood transfusion was also independently associated with HCV (OR=8.3, 95% CI: 2.1-32.0). Plasma donors had higher risk than whole blood donors (OR=7.6, 95% CI: 2.9-20.9); female donors had lower risk than male donors (OR=0.32, 95% CI: 0.12-0.80). The strength of the association between selling blood and HIV infection was lower when plasma donors were excluded (OR=8.0 versus 14.4). Illegal plasma/blood donation practices led to high HCV risk for donors in the 1980s and 1990s. Failure to screen for HCV increased risk for transfusion recipients in this same time period. China has taken steps to battle illegal blood collection and to improve blood banking. However, there will be an ongoing challenge to care for HCV patients even as incidence declines.

INTRODUCTION

Global prevalence of hepatitis C virus (HCV) varies widely, from <1% in Hong Kong (China) or Sweden to >14% in Egypt and Cameroon [1]. An estimated 3.2% of persons in mainland China are infected with HCV [2]. Percutaneous exposures, including reuse of needles and syringes, injection drug use (IDU), and transfusion of unscreened blood

products, are well-established risk factors. Two Chinese studies published in 2004 showed that more than 70% of IDUs in Sichuan and Guangxi provinces were HCV antibody positive [3, 4], comparable to the 60% portion of cases attributable to IDU in the United States [3]. The risk of HCV through blood transfusion is now significantly reduced by screening transfused blood and identifying donor risk behaviors in most industrialized countries. However, in resource-limited developing countries, transmission of HCV by blood transfusion or medical reuse of needles and syringes remains a serious public health problem [6, 7].

The first major HCV outbreak documented in China was reported in 1985 among plasma donors [8]. During the late 1980s and early 1990s, illegal commercial plasma collection was common in selected rural areas of central China. Pooling blood and reinfusing red blood cells of the compatible blood type into donors were done to avoid anemia and to permit more frequent donation from the same donors. Several blood-borne diseases were thus transmitted efficiently, including HCV and human immunodeficiency virus (HIV). A high prevalence of HCV was observed among plasma donors in Hebei, Shandong, Hunan, Hubei, Henan, and even in Beijing [8-12]. In the late 1990s, illegal plasma collection practice was reduced markedly by government legal action. We conducted a community-based epidemiologic study to evaluate the extent of HCV infection among residents in communities where illegal plasma donation had been documented and to explore the risk factors associated with infection.

METHODS

Study Context

This study was an epidemiologic survey conducted for planning purpose as part of a larger, ongoing project, China Integrated Programs for Research on AIDS (China-CIPRA) led by the Chinese Center for Disease Control and Prevention. China-CIPRA comprises 5 integrated sub-projects and 4 supporting cores (figure 1). Our study estimated prevalence and risk factors for HCV among residents in former plasma donating communities in Shanxi Province. The study protocol was approved by the institutional review boards of the Chinese National Center for AIDS/STD Prevention and Control and the University of Alabama at Birmingham, and by the Division of AIDS Prevention Science Review Committee of National Institute of Allergy and Infectious Diseases,

Study Site and Subjects

Shanxi Province is located in central China and borders Henan Province in the south, which has the most severe HIV epidemic caused by unhygienic plasma collection. Of the total 644 HIV infections reported during 1995 and 2003, 76% were associated with blood/plasma collection [13]. A township in southern part of Shanxi Province was selected as the study site based on the following factors: (1) an illegal commercial plasma collection station had operated there around 1995; (2) many HIV-infected persons were reported by local health officials. Twelve out of the 25 villages in the township were selected based on their history of previous illegal plasma and blood collection practices and the willingness to collaborate of village leaders. A roster of all residents in the study residents in the study villages was obtained from local authorities. This population roster

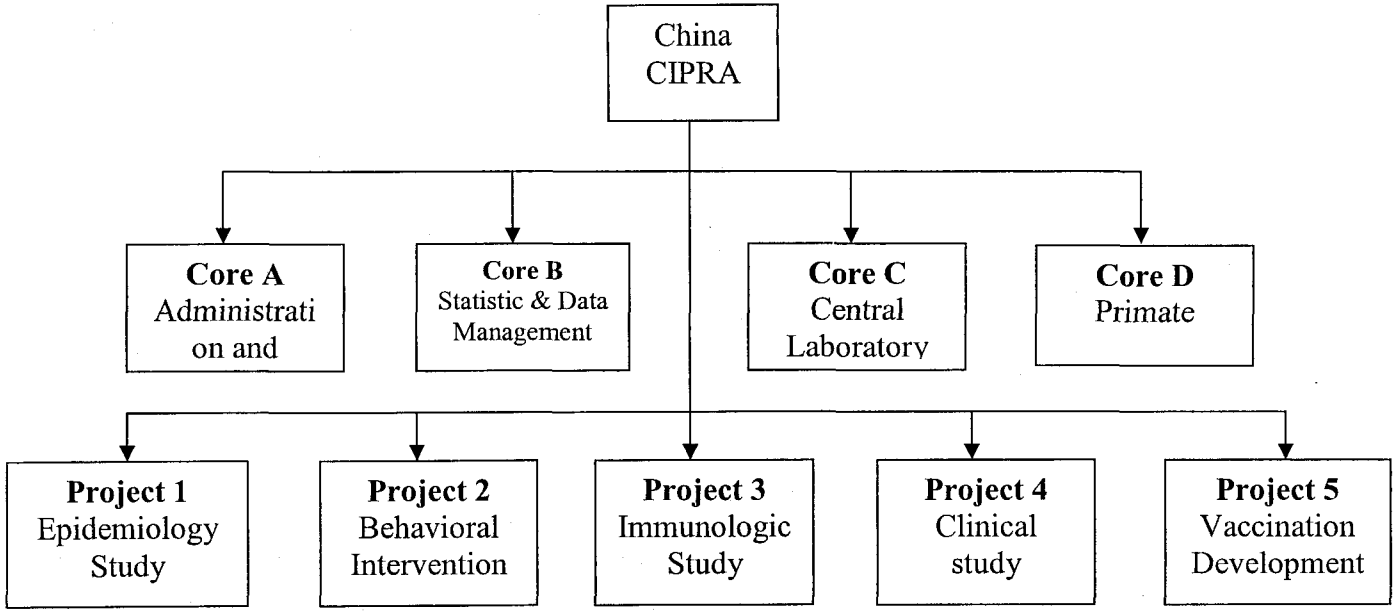

Figure 1. Structure of China-CIPRA Project

was updated with the help of village leaders by adding new residents and excluding those who had died or permanently moved out of the villages.

Based on the final roster of adult villagers, a random sample of 660 villagers was obtained from a sampling frame of 9205 villagers. Inclusion criteria were as follows: (1) permanent resident, having lived in one of the target villages continuously for at least 6 months; (2) age 18-59 years; (3) able and willing to provide informed consent; (4) able and willing to provide contact information. The study was conducted in November and December 2003.

Data Collection

Standardized questionnaire interviews were administered by same-sex, trained interviewers who collected demographic and medical history; behavioral data, including blood donation history; and knowledge, attitudes, and behavioral data. Venous blood was collected for testing of HCV antibody using an enzyme immuno-absorbent assay (EIA) (DiaSorin S.P.A., Suyog Diagnostics Pvt. Ltd., Italy). Individual pre-test counseling was provided to all participants by same-sex, trained counselors. Participants received 15 Chinese Yuan (approximate U.S. $1.80) for their travel expenses and time taken from work after they completed the study visit. Questionnaire completion and laboratory testing were monitored by internal and external quality controls.

Statistical Analysis

Original questionnaire and laboratory testing data were entered into and managed by a DataFax system (Clinical DataFax Systems Inc., Hamilton, ON, Canada), then trans-

ferred into a SAS (SAS Institute Inc., Cary, NC) database for analysis. HCV seroprevalence rates were calculated for all subjects and for sub-groups of former plasma/blood donors (FPDs) and non-FPDs. Fisher's exact 95% confidence intervals (CIs) for point estimates were obtained based on the assumption of binomial distributions. Univariate logistic analysis was first used to explore associations with HCV infection. Variables that were significant in the univariate model ($P \leq 0.05$) were included in a multivariable logistic regression model. Those variables not significant in the multivariable model were eliminated in a stage-wise manner, identifying variables that were independently associated with HCV seropositivity. In order to explore the association of HCV infection with the characteristics of commercial blood donation activities, separate sub-group analyses were also performed for FPDs. All probability values were reported as 2-sided.

RESULTS

Recruitment Rates

With the assistance of village leaders, 87.6% (578/660) of selected villagers were contacted successfully; three (0.5%) were ineligible, and 35 (6.1%) refused to participate. Two persons (0.3%) refused to permit blood to be drawn, such that 538 subjects were included in this analysis (figure 2). Nonparticipants (58% males, 71/122) had a similar sex distribution as the participants (50% males, 268/538) ($P = 0.091$), but nonparticipants (48% less than 30 years old, 59/122) were younger than participants (20%, 110/538) ($P < 0.001$).

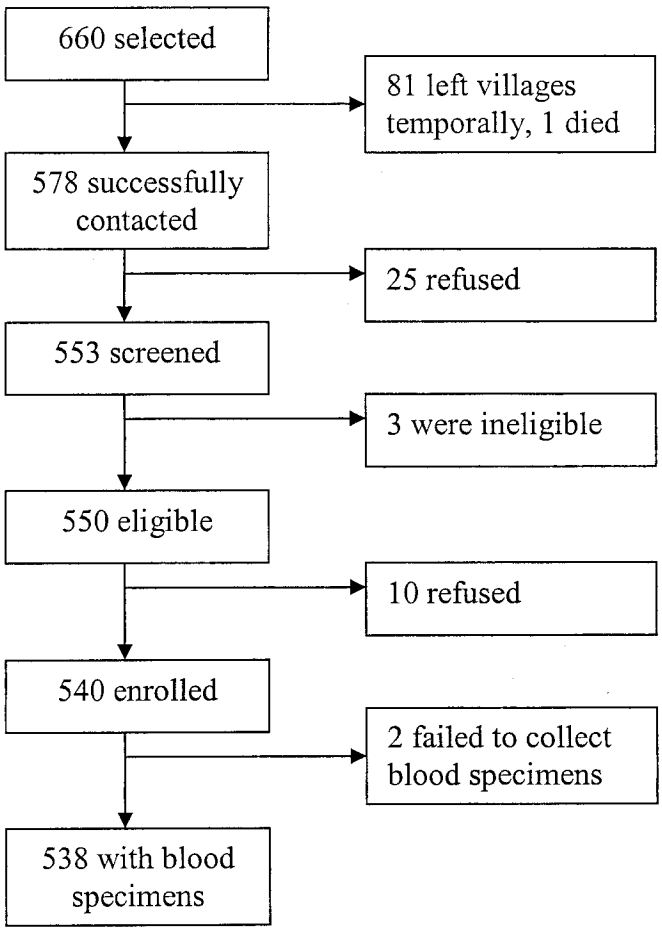

Figure 2. Screening and enrollment of subjects

Commercial Blood/Plasma Donation

Among 538 villagers, 119 (22.1%) had a history of selling blood or plasma: 91 (16.9%) sold whole blood only, 7 (1.3%) sold plasma only, and 21 (3.9%) sold both. The prevalence rates of commercial plasma/blood donation in 12 villages ranged from 8.8% to 48.7% per village. The most common reasons for selling plasma/blood were a need for money (60.5%, 72/119) and being convinced by other people (38.7%, 46/119). Villagers began to sell blood as early as in 1973 and as late as 1998; 60% of the 538 villagers donated from 1990 to 1995. No villager reported selling plasma or blood after 1998; the main reasons for stopping paid donations were their improved economic status (16.8%, 20/119), concern about harm of blood drawing on health (16.8%, 20/119), not being qualified any more (15.1%, 18/119), and the closure of the illegal blood center (15.1%, 18/119). While 46.2% of FPDs had sold plasma/blood for 2 to 9 times in their lifetimes, 3.4% reported donating ≥100 times. The institutions where plasma/blood was sold included official blood collection centers (79.8%), "underground" or illegal plasma collection centers (23.5%), and government hospitals (17.6%). Of former donors, 82.4% sold plasma/blood outside their home Wenxi County.

HCV Prevalence and Risk Factors

Anti-HCV antibodies were detected in 44 persons, a prevalence rate of 8.2% (95% CI: 4.4%-10.9%). Among former donors, 27.7% (33/119) were infected (95% CI: 19.9%-29.3%), and among nondonors, 2.6% (11/419) were infected (95% CI: 1.3%-4.7%).

In univariate analyses, villagers ages ≥35 years old had higher HCV seroprevalence than those < 35 years old (table 1). There was a significant positive trend for HCV seropositivity and age (P <0.001). Villagers who had attended middle school or higher school levels had lower HCV seroprevalence than those who attended elementary school or had no education (P = 0.003). HCV seropositivity was also associated with a history of selling blood or plasma, multiple lifetime sexual partners, and a history of blood transfusion. Multivariable logistic analyses demonstrated that villagers who had ever sold blood or plasma (OR=14.4, 95% CI: 7.1, 31.6) or who had received a blood transfusion (OR=8.3, 95% CI: 2.1, 32.0) were far more likely to be HCV positive. An association of HCV infection and having had multiple sexual partners was suggested (OR=2.4, 95% CI: 0.94, 5.6) (table 1).

In our subgroup analysis of 119 former plasma or blood donors, univariate analyses suggested that HCV infection was associated with male sex, selling plasma, selling plasma and/or blood in official blood centers, multiple lifetime sexual partners, and blood transfusion (table 2). Only male sex and selling plasma were significant in the multivarible logistic regression model. Female donors were less likely to be HCV seropositive (OR=0.32, 95% CI: 0.12, 0.80). Donors of plasma had a higher HCV risk than donors who only donated whole blood (OR=7.6, 95% CI: 2.9, 20.9).

The odds of having donated plasma if one has HCV was 7.6 times greater than the odds of having donated blood (table 2). When we reran our logistic model excluding the 28 persons who said that they had donated plasma, the risk factors stayed the same (data not shown), but the odds ratio for blood donation was 8.0 (95% CI: 3.6, 18.6) compared to OR=14.4 when plasma and/or blood donors were included in the full model.

Table 1. Factors associated with HCV infection in 538 residents of former commercial blood donating communities in rural Shanxi Province, China.

Factors	No. (% HCV positive)	Unadjusted Odds Ratio	*P*-value	Adjusted Odds Ratio [a]	*P*-value
Sex					
Male	268 (10.1)	1.0			
Female	270 (6.3)	0.60 (0.3, 1.2)	0.11		
Age					
< 35 years	185 (1.6)	1.0			
≥35 years	353 (11.6)	8.0 (2.9, 33.3)	<0.001		
Marriage					
Single	21 (0.0)	1.0			
Married	517 (8.5)	b	b		
Occupation (all were farmers)					
Having no other incomes	172 (6.4)	1.0			
Having other incomes	366 (9.0)	1.5 (0.74, 3.1)	0.30		
Education					
Elementary or lower	130 (14.6)	1.0			
Middle or higher	408 (6.1)	0.38 (0.2,0.73)	0.003		
History of selling blood or plasma					
No	419 (2.6)	1.0		1.0	
Yes	119 (27.7)	14.2 (7.1,30.5)	<0.001	14.4(7.1,31.6)	<0.001
No. lifetime sexual partners					
≤1	473 (7.2)	1.0		1.0	
> 1	65 (15.4)	2.4 (1.05, 4.9)	0.027	2.4 (0.94, 5.6)	0.058
Illicit drug use					
No	536 (8.2)	1.0			
Yes	2 (0.0)	b	b		
History of tooth extraction					
No	403 (7.0)	1.0			
Yes	135 (11.9)	1.8 (0.93, 3.4)	0.075		
History of acupuncture					
No	507 (7.9)	1.0			
Yes	31 (12.9)	1.7 (0.49, 4.7)	0.33		
History of surgical operation					
No	501 (7.8)	1.0			
Yes	37 (13.5)	1.9 (0.61, 4.7)	0.23		

Table 1. (Continued)

Factors	No. (% HCV positive)	Unadjusted Odds Ratio	*P*-value	Adjusted Odds Ratio[a]	*P*-value
History of blood transfusion					
No	523 (7.3)	1.0		1.0	
Yes	15 (40.0)	8.5 (2.7, 24.9)	<0.001	8.3 (2.1, 32.0)	0.003
History of medical injection [c]					
No	120 (5.8)	1.0			
Yes	418 (8.5)	1.6 (0.72, 3.9)	0.29		

NOTE. [a] Multivariate logistic regression analysis using variables significant at the $P \leq 0.05$ level in the univariate models.
[b] No definition.
[c] Intravenous or intramuscular use of medicines for treating diseases

Table 2. Factors associated with HCV seroprevalence in 119 former commercial plasma and/or blood donors in rural Shanxi Province, China.

Factors	No. (% HCV positive)	Unadjusted Odds Ratio	*P*-value	Adjusted Odds Ratio [a]	*P*-value
Sex					
Male	61 (37.7)	1.0		1.0	
Female	58 (17.2)	0.34(0.14, 0.8)	0.015	0.3 (0.12, 0.8)	0.018
Occupation (all were farmers)					
Having no other incomes	39 (20.5)	1.0			
Having other Incomes	80 31.3)	1.8 (0.73, 4.6)	0.22		
Education					
Elementary or lower	48 (35.4)	1.0			
Middle or higher	71 (31.3)	0.53 (0.23,1.2)	0.13		
Ever sold plasma					
No	91 (17.6)	1.0		1.0	
Yes	28 (60.7)	7.2 (2.9, 18.9)	<0.001	7.6 (2.9, 20.9)	<0.001
Selling blood during 1991-1995					
No	47 (25.5)	1.0			
Yes	72 (29.2)	1.2 (0.53, 2.8)	0.67		

Table 2. (Continued)

Factors	No. (% HCV positive)	Unadjusted Odds Ratio	*P*-value	Adjusted Odds Ratio [a]	*P*-value
Frequency of selling blood					
< 10 times	74 (24.3)	1.0			
≥10 times	45 (33.3)	1.6 (0.68, 3.5)	0.29		
Sold at underground blood centers					
No	91 (28.6)	1.0			
Yes	28 (25.0)	0.83 (0.3, 2.1)	0.71		
Sold at official blood centers					
No	24 (8.3)	1.0			
Yes	95 (32.6)	5.3 (1.4, 34.6)	0.03		
Sold at government hospitals					
No	98 (25.5)	1.0			
Yes	21 (38.1)	1.8 (0.65, 4.8)	0.25		
No. lifetime sexual partners					
≤1	103(24.3)	1.0			
> 1	16 (50.0)	3.1 (1.05, 9.3)	0.04		
History of teeth extraction					
No	83 (25.3)	1.0			
Yes	36 (33.3)	1.5 (0.62, 3.4)	0.37		
History of acupuncture					
No	111(26.1)	1.0			
Yes	8 (50.0)	2.8 (0.63,12.7)	0.16		
History of surgical operation					
No	108(25.9)	1.0			
Yes	11 (45.5)	2.4 (0.64, 8.5)	0.18		
History of blood transfusion					
No	113(25.7)	1.0			
Yes	6 (66.7)	5.8 (1.1, 43.4)			
			0.049		
History of medical injection [b]					
No	33 (15.2)	1.0			
Yes	86 32.6)	2.7 (0.94, 7.8)			
			0.064		

NOTE. [a] Multivariate logistic regression analysis using variables significant at the $P \leq 0.05$ level in the univariate models.

[b] Intravenous or intramuscular use of medicines for treating diseases.

DISCUSSION

This community-based cross-sectional study in rural former commercial plasma or blood donating communities in China found high HCV seroprevalence rates. Among villagers age 18-59 years old, 8.2% were infected. Among those with a history of selling blood or plasma, 27.7% were HCV antibody positive, while HCV seroprevalence among nondonors was 2.6%, similar to that in the general population of China [2, 14]. Selling blood/plasma was the strongest predictor for being HCV seropositive among the villagers in the rural communities of Shanxi Province; the risk among donors was 14.4 times higher than nondonors after adjusting for other confounding factors. Among former donors, those who had donated plasma had 7.6 times the risk of HCV than those who had donated whole blood only. Caution should be taken in interpreting any association of HCV with whole blood donation. Plasma donation is more stigmatized than blood donation in the study communities, as local residents logically relate plasma donation, where erythrocytes were reinfused, with risk of HIV infection. Some plasma donors may have reported themselves as blood donors, the so-called social desirability bias [15]. We did not observe an association of the type of blood collection center with HCV infection, unlike the association reported elsewhere of illegal private blood collection center and HIV infection [16]. Whether this reflects the poor memories persons have of the type of donation center or whether there were also blood hygiene problems in government blood bank services is not known.

Exposure to contaminated blood or blood products is the major risk factor for HCV infection; sexual transmission of HCV is far less efficient [17]. A prospective study reported that persons in long-term monogamous partnerships had a risk of 0% to 0.6%

per year for HCV seroconversion, while persons with multiple partners or those at risk for sexually transmitted diseases had a risk of 0.4% to 1.8% per year [18]. Our study showed that villagers who received blood transfusion had about 8 times of risk for HCV seropositivity than those who had no history of blood transfusion, suggesting the vital need for local blood banks to screen all blood products for HCV. Villagers with >1 lifetime sexual partner also had a higher risk of HCV seropositivity than those with ≤1 sexual partner ($P = 0.058$). Further studies with larger sample sizes would be needed to confirm any independent association of multiple sexual partners and HCV infection in these communities.

Older age and lower education were associated with HCV seropositivity in univariate analyses, but these associations were not significant in multivariate analysis. These observations may be related to a cohort effect. Commercial plasma donation practice was prevalent about 10 years before our survey was conducted. A majority of villagers who sold plasma/blood in the early 1990s were older by the time of our 2003 survey. They also have a lower educational level than does the younger generation. It is likely that selling plasma or receiving blood transfusion is the risk factor of importance, with age and education associated with the exposure, not the outcome per se. Among those who reported a history of selling plasma/blood, females had a lower risk than males. No biological mechanism has been reported to suggest that males are more vulnerable to HCV infection; this difference of HCV prevalence between sexes might imply unmeasured risks for male former blood donors.

Our community-based survey had a number of methodological strengths. We conducted a community census from which a random sample was drawn. The study was

well explained to the villagers during the Village Health Camp before the study and during individual informed consent, and the participation was high even though it was totally voluntary. A majority of nonparticipations were due to temporary out-migration, and only 6% of these contacted villagers refused. Given China's extensive health care networks, extending to the village level, our experience suggests that good epidemiologic studies can be undertaken even in rural China in collaboration with local public health departments and community leaders. Our study also had limitations. We did not successfully identify communities with high HIV infection rates (only 7 of 538 [or 1.3%] were HIV infected), making our study of risk for HIV infection impossible. Our study was conducted about a decade after the exposures occurred, so death and out-migration may have altered our findings. HIV-related deaths may lead to underestimation of HCV prevalence, as HCV shares a blood transmission route with HIV. Nonparticipants were younger than participants and less likely to have been infected with HCV though plasma donation; a majority of the nonparticipants were temporary out-migrants (81/120) and may have been more likely to practice risk behaviors, such as using illicit drugs or commercial sex. Therefore, a lack of data regarding nonparticipants may bias the estimate of HCV prevalence in either direction. Nonetheless, we believe that our evidence is strong to indicate that unhygienic plasma donation and receipt of blood transfusion have been strong risk factors for HCV infection in rural central China. Improved blood collection and blood banking practices are an urgent health priority.

REFERENCES

1. Koff RS. Hepatitis C. In: Gorbach SL, Bartlett JG, Blacklow NR, eds. Infectious Diseases. 2nd ed. Philadelphia: W.B. Saunders Company, **1998**: 864–71.

2. Liu CB. [Epidemic and risk factors of viral hepatitis in general population in China]. Zhongguo Gan Bing Za Zhi **1998;** 6:67-70.

3. Yuan YH, Hong KX, Liu SZ, et al. Community-based survey of HCV and HIV coinfection in injection drug abusers in Sichuan Province of China. World J Gastroenterol **2004;** 10:1589-93.

4. Garten RJ, Lai SH, Zhang JB, et al. Rapid transmission of hepatitis C virus among young injecting heroin users in Southern China. Intl J Epidemiol **2004;** 33:182-8.

5. United States Center for Disease Control and Prevention. National Hepatitis C Prevention Strategy. Available at: http:/www.cdc.gov/ncidod/diseases/hepatitis/c/plan/HCV_infection.htm (Accessed 18 March 2005).

6. Chandra M, Khaja MN, Farees N, et al. Prevalence, risk factors and genotype distribution of HCV and HBV infection in the tribal population: a community based study in south India. Trop Gastroenterol **2003;** 24:193-5.

7. Frank C, Mohamed MK, Strickland GT, et al. The role of parenteral antischistosomal therapy in the spread of hepatitis C virus in Egypt. Lancet **2000;** 355:887-9.

8. Meng DA. Serological study on hepatitis C infection in plasma donors. Zhonghua Yu Fang Yi Xue Za Zhi **1990;** 24:193-5.

9. Chen X, He JM, Wu HQ, et al. A seroepidemiological and behaviour factors study of HIV, HCV, HBV and syphilis infection among commercial blood donors. Shi Yong Yu Fang Yi Xue **1999;** 6:174-6.

10. Liu SZ, Fu JH, Cui YH, et al. A study on prevalence and subtypes of hepatitis C virus among blood donors in some areas of Shandong Province. Zhongguo Gong Gong Wei Sheng **2000;** 16:527-8.

11. Zhang SY. Conditional logistic regression analysis of the influential factors of HCV infection in one blood donator aggregated village. Yu Fang Yi Xue Wen Xiang Xin Xi **2000;** 6:3-4.

12. Yin N, Mei S, Li L, et al. Study on the epidemiology and distribution of human immunodeficiency virus-1 and hepatitis C virus infection among intravenous drug users and illegal blood donors in China. Zhonghua Liu Xing Bing Xue Za Zhi **2003;** 24:962-5.

13. Qiao XC, Nie XY, Guo XL. Analysis of the epidemic of HIV/AIDS in Shanxi province and the strategy for HIV/AIDS prevention and control. Zhongguo Xing Bing Ai Zi Bing Fang Zhi **2004**;10:190-2.

14. Ding X, Gu H, Zhong ZH, et al. Molecular epidemiology of hepatitis viruses and genotypic distribution of hepatitis B and C viruses in Harbin, China. Jpn J Infect Dis **2003;** 56:19-22.

15. Lau JT, Tsui HY, Wang QS. Effects of two telephone survey methods on the level of reported risk behaviours. Sex Transm Infect. **2003;** 79:325-31.

16. Chen H, Qian X, Cao GH, et al. Study on the seropositive prevalence of human immunodeficiency virus in a village residents living in rural region of central China. Zhonghua Liu Xing Bing Xue Za Zhi. **2004;** 25:317-21.

17. Brook MG. Sexually acquired hepatitis. Sex Transm Infect **2002;** 78:235-40.

18. Terrault NA. Sexual activity as a risk factor for hepatitis C. Hepatol **2002;** 36:S99-S105.

PREVALENCE AND RISK FACTORS FOR HIV AND HEPATITIS C VIRUS COINFECTION IN RURAL CHINESE COMMUNITIES WITH FORMER PLASMA DONORS

by

HANZHU QIAN, STEN H. VERMUND, RICHARD A. KASLOW, CHRISTOPHER S. COFFEY, ERIC CHAMOT, YAN JIANG, XIAOCHUN QIAO, YULIANG ZHANG, XIAOMING SHI, ZHONGMIN YANG, AND NING WANG

In preparation for *AIDS*

Format adapted for dissertation

ABSTRACT

Illegal paid plasma donation activities in the late 1980s and early 1990s caused many HIV and HCV infections in rural China due to the use of unsterilized equipment and reinfusing pooled red blood cells to donors. In order to estimate the prevalence of HIV and HCV coinfections, and to investigate the risk factors, a cross-sectional study was conducted among adult residents in rural Shanxi Province, China. Blood samples were collected for testing of HIV and HCV antibodies; a structured questionnaire was administered. Risk factors were explored with Cochran-Armitage trend tests and ordinal logistic regression models. Of 3062 participating villagers, 29.5% reported a history of selling whole blood or plasma, and 8.3% had ever sold plasma alone. HIV seoropositivity was confirmed by Western blot in 1.3% of subjects, while 12.7% were HCV antibody positive. The coinfection rates of HIV and HCV were 1.1% among all study subjects, 85% among HIV positive subjects, and 8.7% among HCV positive subjects. Factors associated with coinfection were residence in a village with a prior illegal plasma collection center (OR=2.7, 95% CI: 2.1, 3.5), male sex (OR=7.7, 95% CI: 3.8, 15.8), older age (OR=1.6, 95% CI: 1.2, 2.0), lower education (OR=1.4, 95% CI: 1.1, 1.8), and a history of selling plasma (OR=14.1, 95% CI: 10.5, 18.9). Having a spouse infected with HIV or HCV was also significantly associated with coinfection. HCV infection must be considered as HIV prevention and treatment projects are launched in rural China.

INTRODUCTION

During the late 1980s and early 1990s, illegal commercial plasma/blood collection was common in selected rural areas of central and eastern China; the practice of

pooling blood and reinfusing red blood cells into donors of the same blood types caused a rapid spread of several blood-borne diseases, including hepatitis C virus (HCV) and human immunodeficiency virus (HIV) infections [1-3]. The high baseline prevalence of hepatitis B in the general population of China has not been associated closely with illegal plasma donation [2, 4]. The first recognized outbreak of HCV infection among plasma donors occurred in 1985 [1]. Since then, several studies have investigated HCV infection among former plasma or blood donors (FPDs), in whom a prevalence of 17.1% to 72.8% has been documented [2, 5, 6]. The spread of HIV among FPDs was first identified around 1995 [7]. In subsequent epidemiologic studies HIV prevalence ranged from 0.2% to 56.1% among FPDs in village surveys from areas with known illegal plasma donation practices [2-4, 8]. Prior studies suggest that 68%-87% of HIV-positive FPDs were coinfected with HCV [4, 9], but these did not represent community samples.

Due to shared risk factors for transmission, coinfection with HIV and HCV is common [4, 9]. Several studies suggested that HIV coinfection can accelerate the natural course of chronic hepatitis C, increase the risks for liver cirrhosis and hepatocellular carcinoma, and cause decompensated liver disease [10, 11]. Other studies have shown an increased risk of progression to acquired immunodeficiency syndrome (AIDS) and AIDS-related death among HIV-HCV-positive persons, suggesting that HCV coinfection may accelerate the course of HIV disease [12, 13]. In addition, hepatitis C infection may affect the management of HIV infection by increasing the incidence of liver toxicity associated with certain antiretroviral regimens [14, 15]. For all of the above reasons, we undertook the current study among rural Chinese communities with FPDs and HIV/AIDS

cases to estimate the prevalence of HIV and HCV coinfection and to characterize risk factors.

METHODS

This cross-sectional study was conducted in southern Shanxi Province, near Henan Province, the epicenter of HIV/AIDS acquired through unsanitary plasma collection. A pilot study among 538 randomly selected adult villagers from 12 villages found that 1.3% participants were infected with HIV, and 8.2% were infected with HCV (Hanzhu Qian, unpublished data). Four of these 12 villages were selected based on the basis of both the willingness of village leaders to collaborate and the higher frequency of plasma or blood donation in the pilot study.

All of the 3718 villagers aged 18 to 64 years in these 4 villages were invited to participate in this study in May and August 2004. Standardized questionnaire interviews administered by same-sex, trained interviewers sought demographic and medical histories and behavioral data, including blood donation history. Venous blood was collected for testing of HIV and HCV antibodies. Each blood sample was screened by enzyme-linked immunosorbent assay (ELISA) (GBI Biotech Co., Ltd., Beijing, China) for HIV antibody, and positive tests were confirmed by HIV-1/2 Western Blot immune assay (HIV Blot 2.2 WB, Genelabs Diagnostics, Singapore). HCV antibody was tested using enzyme immuno-absorbent assay (EIA) (DiaSorin S.P.A., Suyog Diagnostics Pvt. Ltd., Italy). Individual pre- and post-test counseling was provided to all participants. Before any study data were solicited, written informed consent was obtained from each participant. The study protocol was approved by institutional review boards of the Chinese National Cen-

ter for AIDS/STD Prevention and Control and the University of Alabama at Birmingham, and by the National Institute of Allergy and Infectious Diseases.

Statistical analysis was performed using SAS version 9.0 (SAS Institute Inc., Cary, NC). The point prevalence of HIV and HCV infection was calculated and compared between plasma/blood donors and nondonors. The Cochran-Armitage trend test was performed to compare trends between 3 groups of subjects: HIV- and HCV- coinfected, monoinfected, and negative subjects. Ordinal logistic regression (cumulative logit model) of the trichotomous dependent variable (coinfection, monoinfection, or no infection) was undertaken to adjust for a number of covariates of sociodemographic and risk factors associated with infection status. Ordinal logistic models were also fit in a subgroup of male and female subjects separately to explore the association of HIV or HCV status of the spouse with coinfection. Test results were considered significant for association with a two-sided P value of < 0.05.

RESULTS

Of the 3718 villagers, 3602 (82.4%) participated in the study and contributed blood samples for HIV and HCV testing, and were therefore included in this analysis. Nonparticipants were younger (36.7% less than 30 years old, 241/656) than participants (17.8%, 550/3062), and more likely to have never been married (11.6% single, 76/654) than participants (3.8%, 116/3062), but similar in sex distribution and educational level.

Among the 3602 participants, 50% were males; 70.7% had attended middle school or above; 96.2% were married; all participants were Han majority ethnicity; 53.9% had other incomes in addition to farming; the mean age was 41 years old; and

29.5% (904/3062) had a history of selling plasma or blood (1.2% plasma only, 21.2% whole blood only, and 7.1% both). Those who had ever donated plasma accounted for 8.3% of all participating villagers.

HIV seropositivity was detected in 40 (1.3%) villagers; HIV seroprevalence in those who sold blood or plasma was 30 times higher than in those who did not (P <0.001). HCV seropositivity was detected among 389 (12.7%) villagers; donors had nearly 10 times of risks than nondonors (P <0.001). All 34 (1.1%) HIV- and HCV-coinfected villagers were FPDs (table 1). Of the 40 HIV-infected villagers; 85% were HCV antibody positive; of the 389 HCV-infected villagers, 8.7% were coinfected with HIV.

Table 1. HIV and HCV infections in former plasma/blood donating communities in Shanxi Province, China.

Infection	Donors (n=904, %)	Non-donors (n=2158, %)	OR (95% CI)	P
HIV	37 (4.1)	3 (0.14)	30.7 (11.1, 127)	< 0.001
HCV	288 (31.9)	101 (4.7)	9.5 (7.5, 12.2)	< 0.001
HIV and HCV	34 (3.8)	0 (0.0)	Not defined	<0.001*

NOTE. OR=odds ratio; CI=confidence interval. * Fisher's exact test.

There were significant trends for association across the 3 infection categories (dually, singly, and not infected) for residence in a village with a plasma collection center in the mid-1990s (P < 0.001), male sex (P < 0.001), low education level (≤6 years of school) (P < 0.001), older age (≥30 years) (P < 0.001), history of selling plasma (P < 0.001), and history of dental extraction (P < 0.001) (table 2). There was no trend for association with being married or history of donating only whole blood, though these two variables were statistically significant (table 2).

Table 2. Factors associated with HIV-HCV coinfected, mono-infected, and non-infected status among villagers in rural Shanxi Province, China.

Factor	Coinfected (34, 1.1%)	Monoinfected (361, 11.8%) [§]	Non-infected (2667, 87.1%)	P^*
Village with a plasma collection center	20 (58.8)	203 (56.2)	778 (29.2)	<0.001
Male	24 (70.6%)	200 (55.4%)	1306 (49.0%)	0.001
Education (≤6 years)	19 (55.9%)	149 (41.3%)	728 (27.3%)	<0.001
Age (≥30 years)	34 (100.0)	353 (97.8)	2125 (79.7)	<0.001
Marriage (ever married)	33 (97.1%)	357 (98.9%)	2556 (95.8%)	0.01 ‡
Occupation (have other incomes)	20 (58.8%)	173 (47.9%)	1457 (54.6%)	0.08
History of selling plasma	25 (73.5%)	138 (38.2%)	91 (3.4%)	<0.001
History of selling whole blood only	9 (26.5%)	119 (33.0%)	522 (19.6%)	<0.001‡
No. lifetime sexual partners, mean(SD)†	1.4 (1.9)	1.2 (0.6)	1.2 (1.5)	0.69
Illicit drug use	0 (0.0%)	3 (0.8%)	9 (0.3%)	0.31
History of dental extraction	13 (38.2%)	134 (37.1%)	784 (29.4%)	0.002
History of acupuncture	2 (5.9%)	23 (6.4%)	131 (4.9)	0.26
History of surgical operation	0 (0.0%)	32 (8.9%)	194 (7.3)	0.95
History of blood transfusion	0 (0.0%)	9 (2.5%)	3 (1.2)	0.20
History of medical injection	24 (70.6%)	244 (67.6%)	1919 (72.0)	0.13

NOTE. [§] Monoinfected = (HCV only, N=355 [11.6%] or HIV only, N=6 [0.2%]);
[*] Cochran-Armitage trend test.
[†] by ANOVA.
[‡] Group proportions differ significantly, but not a trend association.

The six factors showing a significant trend in the Cochran-Armitage trend test were included in ordinal logistic regression models comparing multivariable association across the 3 infection categories. Adjusted associations with the trends toward dual infec-

tion that remained significant were residence, male sex, older age, low education level, and history of selling plasma. Ordinal logistic regression models were also fit separately for male and female subjects. Residence, age, and history of selling plasma were independently associated with a trend toward coinfection in both male and female subjects. The association with the trend toward coinfection in both men and women were particularly strong when the spouse was HIV infected and weaker but still significant when the spouse had an HCV infection (table 3).

Table 3. Factors associated with HIV-HCV coinfected, mono-infected, and non-infected status among villagers in rural Shanxi Province, China, as predicted by cumulative logit models.

Infection	Among all subjects Adjusted OR (95% CI)	Among males Adjusted OR (95% CI)	Among females Adjusted OR (95% CI)
Residing in a village with an illegal plasma collection center	2.7 (2.1, 3.5)	3.5 (2.4, 5.0)	1.6 (1.05, 2.5)
Male	7.7 (3.8, 15.8)	NA	NA
Age (≥30 years)	1.6 (1.2, 2.0)	8.8 (2.7, 53.8)	4.4 (1.6, 18.1)
Education (≤6 years)	1.4 (1.1, 1.8)	1.6 (1.1, 2.5)	-
History of selling plasma	14.1 (10.5, 18.9)	13.2 (8.3, 21.3)	9.7 (6.0, 15.7)
HIV positive spouse	NA	12.0 (2.9, 54.1)	9.6 (3.2, 30.1)
HCV positive spouse	NA	2.4 (1.5, 3.7)	2.4 (1.5, 3.8)

NOTE. OR=odds ratio; CI=confidence interval; NA=not applicable.

DISCUSSION

Our community-based study showed a higher prevalence of HCV infection (12.7%) among residents in the rural communities where illegal plasma and blood collection was common in the mid-1990s, compared to 3.2% in the general population in mainland China [16]. A moderate prevalence (for China) of HIV infection (1.3%) was found in this study, lower than those in other village surveys in Chinese plasma donating communities [2-4, 8]. Eighty five percent of HIV-infected villagers were coinfected with HCV, and 8.7% of HCV-infected villagers were coinfected with HIV. In univariate analyses, increasing trends across the 3 categories of infection toward coinfection were observed for being male, low education, older age, history of selling plasma, history of teeth extraction, or residence. History of unhygienic plasma donation showed a consistently strong association with HIV-HCV coinfection in ordinal multivariable logistic regression models adjusted for other potential risk factors. Residence in a village where an illegal plasma collection center was operated in the mid-1990s and age above 30 years were also independently associated with coinfection. HIV or HCV seropositivity of the spouse was significantly associated with coinfection in sub-group analyses in male and female villagers. We cannot exclude transmission of HIV or HCV through sexual intercourse or other close interpersonal contacts. However, transmission of these viruses via former plasma donation seems more likely in the vast majority of cases.

Our study had several strengths. Over 82% of villagers age 18 to 64 years voluntarily participated in the study, and this age cohort included most of the villagers who sold plasma or blood 10 years ago. The study was limited somewhat by the reluctance of some villagers to participate in the study, usually because of their fears of receiving posi-

tive test results. We conducted the study nearly a decade after the illegal plasma collection practices were widespread in these communities. These factors may have led to underestimation of the prevalence due to differential nonparticipation, out-migration or death. However, nonparticipants tended to be younger than participants, and those less than 30 years old were unlikely to have sold plasma/blood 10 years ago.

In countries where highly active antiretroviral therapy is available, both mortality and incidence of new AIDS-defining disease have declined among people with HIV infection [17, 18]; meanwhile, chronic liver disease has become increasingly prevalent and constitutes a very important cause of morbidity and mortality in the HIV-HCV coinfected population [19]. HIV-HCV coinfection may present an especially daunting medical and public health challenge to the rural Chinese communities affected by this outbreak. About half of the villagers who were infected with HIV a decade ago are estimated to have developed AIDS [20]. Many infected villagers have not received HIV or HCV testing and are unaware of their status; infections will continue to be transmitted via iatrogenically or sexually in these zones, where injection drug use is fortunately rare. The China CARES Project is providing free antiretroviral (ARV) therapy; however, rural areas in China lack facilities and staff to perform laboratory monitoring for side effects of ARV treatment. Our study findings underscore the importance of considering coinfection of HCV while providing HIV treatment and prevention in rural former plasma donation communities.

REFERENCES

1. Meng ZD. A serological study on hepatitis C infection in plasma donors. Zhonghua Yu Fang Yi Xue Za Zhi **1990;** 24:193-5.

2. Chen X, He JM, Wu HQ, et al. A epidemiologic and behavioral study of HIV, HCV, HBV and syphilis infections among commercial blood donors. Shi Yong Yu Fang Yi Xue **1999;** 6:174-6.

3. Wu ZY, Rou KM, Detels D. Prevalence of HIV infection among former commercial plasma donors in rural eastern China. Health Policy Plan **2001;** 16:41-6.

4. Zhang YX. The prevalence of HCV, HIV and HBV among paid blood donors. Lin Chuan Nei Ke Za Zhi **2001;** 18:308-9.

5. Sun Y. Epidemiological and serological study on hepatitis C virus infection in plasmapheresis donors. Zhonghua Liu Xing Bing Xue Za Zhi **1991;** 12:327-30.

6. Zhang SY. Conditional logistic regression analysis of the influential factors of HCV infection in one blood-donator aggregated village. Yu Fang Yi Xue Wen Xian Xin Xi **2000;** 6:3-4.

7. Wu ZY, Liu Z, Detels R. HIV-1 infection in commercial plasma donors in China. Lancet **1995;** 346:61-2.

8. Zheng XW, Wang Z, Xu J, et al. The epidemiological study of HIV infection among paid blood donors in one county of China. Zhonghua Liu Xing Bing Xue Za Zhi **2000;** 21:253-5.

9. Yan JY, Zheng XW, Zhang XF, et al. The survey of prevalence of HIV infection among paid blood donors in one county in China. Zhonghua Liu Xing Bing Xue Za Zhi **2000;** 21:10-3.

10. Soto B, Sanchez-Quijano A, Rodrigo L, et al. Human immunodeficiency virus infection modifies the natural history of chronic parenterally-acquired hepatitis C with an unusually rapid progression to cirrhosis. J Hepatol **1997;** 26:1-5.

11. Benhamou Y, Bochet M, Di Martino V, et al. Liver fibrosis progression in human immunodeficiency virus and hepatitis C virus coinfected patients. The Multivirc Group. Hepatology **1999;** 30:1054-8.

12. De Luca A, Bugarini R, Lepri AC, et al. Coinfection with hepatitis viruses and outcome of initial antiretroviral regimens in previously naive HIV-infected subjects. Arch Intern Med **2002;** 162:2125-32.

13. Greub G, Ledergerber B, Battegay M, et al. Clinical progression, survival, and immune recovery during antiretroviral therapy in patients with HIV-1 and hepatitis C virus coinfection: the Swiss HIV Cohort Study. Lancet **2000;** 356:1800-5.

14. den Brinker M, Wit FW, Wertheim-van Dillen PM, et al. Hepatitis B and C virus co-infection and the risk for hepatotoxicity of highly active antiretroviral therapy in HIV-1 infection. AIDS **2000;** 14:2895-902.

15. Sulkowski MS, Thomas DL, Mehta SH, et al. Hepatotoxicity associated with nevirapine or efavirenz-containing antiretroviral therapy: role of hepatitis C and B infections. Hepatology **2002;** 35:182-9.

16. Liu CB. [Epidemic and risk factors of viral hepatitis in general population in China]. Zhongguo Gan Bing Za Zhi **1998;** 6:67-70.

17. Mocroft A, Ledergerber B, Katlama C, et al. Decline in the AIDS and death rates in the EuroSIDA study: an observational study. Lancet **2003;** 362:22-9.

18. Anonymous. Survival after introduction of HAART in people with known duration of HIV-1 infection. The CASCADE Collaboration. Concerted Action on SeroConversion to AIDS and Death in Europe. Lancet **2000;** 355:1158-9.

19. Telfer P, Sabin C, Devereux H, et al. The progression of HCV-associated liver disease in a cohort of haemophilic patients. Br J Haematol **1994;** 87:555-61.

20. State Council AIDS Working Committee Office and UN Theme Group on HIV/AIDS in China: A Joint Assessment of HIV/AIDS Prevention, Treatment and Care in China (2004). Available at: http://www.unaids.org/zhq (Accessed 18 March 2005).

SUMMARY CONCLUSION

Overview of Results

We reviewed the magnitude of the HIV/AIDS epidemic and the social characteristics and geographic distribution of at-risk groups in China. We analyzed the data from a cross-sectional study conducted in 2003 and 2004 in rural Shanxi Province, China, where 20%-30% of adult villagers sold plasma/blood in the mid 1990s.

Our review showed that the HIV/AIDS epidemic in China is thus far largely concentrated in selected areas and population sub-groups but is on an upward trend. Sub-groups at higher HIV risk are shifting from IDUs and FPDs to female sex workers and their clients, and men who have sex with men. Those already infected people, especially infected rural residents, represent a significant treatment and care challenge in some heavily afflicted areas.

Analysis of the pilot study data from 524 randomly selected adult villagers found that the knowledge of HIV transmission routes and prevention was fairly good, but misconceptions were also common. Discriminatory attitudes were prevalent and were independently associated with lower knowledge of HIV/AIDS, lower education, older age, and married status. HCV seroprevalence rates were 8.2% in all participants, 27.7% in FPDs, and 2.6% in nondonors. Selling plasma/blood and receiving a blood transfusion were independently associated with HCV.

Analysis of the main study data from 3062 villagers showed that HIV seoropositivity was confirmed in 1.3% of subjects, while 12.7% were HCV seropositive.

HIV-HCV coinfection rates were 1.1% in all subjects, 85% in HIV-positive subjects, and 8.7% in HCV-positive subjects. Factors associated with coinfection were history of selling plasma, residence in a village with a prior plasma collection center, male sex, older age, and lower education level.

Strengths

This community-based study had a number of methodological strengths. A community census was conducted in 12 villages, from which a random sample was drawn for the pilot study. In the main study, all adult villagers in 4 of the 12 villages are invited to be screened for eligibility of participating in the study. In the pilot study, the refusal rate was only 6%, while the enrollment rate was over 90%; over 82% of villagers participated in the main study. The age groups of participating villagers included most of the villagers who sold plasma or blood 10 years ago. Large sample size enhanced the precision of estimates of prevalence rates. Voluntary participation, high enrollment rate, confidential interview, and strict quality control increased the validity of the data.

Limitations

Our study also had weaknesses. This study did not successfully identify communities with high HIV infection rates (only 1.3% were HIV infected), which made it impossible for us to estimate the secondary transmissions of HIV from infected FPDs to their spouses, other sexual partners, and general population via sexual, iatrogenic routes — a current public health concern. This study was conducted about a decade after the exposures occurred, so death and out-migration may have altered our findings by resulting

in underestimation of the prevalence rates. Nonetheless, we believe that our evidence is strong enough to indicate that unhygienic blood and plasma donation are important risk factors for HCV infection and its coinfection with HIV in rural central China. Nonparticipation in our study might affect our results; most of nonparticipants left villages seasonally for temporary jobs and might be more exposed to HIV/AIDS educational information, i.e., their misconceptions and discriminatory attitudes might be lower than participants, but non-participation is not likely to imperil our *a prior* hypothesis testing of the relationship between knowledge and attitude. Some villagers might be reluctant to participate in the study because of their fears of positive testing results. However, our data showed that non-\participants tended to be younger than participants; young villagers less than 30 years old were unlikely to have sold plasma/blood 10 years ago.

Implications

The growing epidemic trend of HIV/AIDS underscores the urgency of scaling up interventions among at-risk sub-group populations as well as the need to educate the general population. HCV coinfection is common among HIV-infected villagers, and may facilitate the disease progression of AIDS and worsen the result of ARV therapy of AIDS patients. HCV infection should be considered in HIV intervention and care projects. Misconceptions and discrimination toward persons with HIV/AIDS are prevalent; the negative association between discriminatory attitudes and knowledge suggests that community education to eliminate misconceptions and increase knowledge may help reduce HIV/AIDS stigma and discrimination.

APPENDIX A

UNIVERSITY OF ALABAMA AT BIRMINGHAM INSTITUTIONAL REVIEW BOARD APPROVAL

THE UNIVERSITY OF ALABAMA AT BIRMINGHAM

Institutional Review Board for Human Use

Form 4: IRB Approval Form
Identification and Certification of Research Projects Involving Human Subjects

UAB's Institutional Review Boards for Human Use (IRBs) have an approved Federalwide Assurance with the Office of Human Research Protections (OHRP). The UAB IRBs are also in compliance with 21 CFR Parts 50 and 56 and ICH GCP Guidelines. The Assurance became effective on November 24, 2003 and the approval period is for three years. The Assurance number is FWA00005960.

Principal Investigator: QIAN, HAN-ZHU

Co-Investigator(s):

Protocol Number: **E041116001**

Protocol Title: *Associations of Plasma Donation with Human Immunodeficiency Virus and Hepatitis Virus Infections in Rural Shanxi Province, China*

The above project was reviewed on 11/17/04 The review was conducted in accordance with UAB's Assurance of Compliance approved by the Department of Health and Human Services. This project qualifies as an exemption as defined in 45CF46.101, paragraph 4.

This project received EXEMPT review.

IRB Approval Date: 11/17/04

Date IRB Approval Issued: 11-17-04

Sheila Moore, CIP

Sheila Moore, CIP
Director, Office of the Institutional
Review Board for Human Use (IRB)

Investigators please note:

IRB approval is given for one year unless otherwise noted. For projects subject to annual review research activities may not continue past the one year anniversary of the IRB approval date.

Any modifications in the study methodology, protocol and/or consent form must be submitted for review and approval to the IRB prior to implementation.

Adverse Events and/or unanticipated risks to subjects or others at UAB or other participating institutions must be reported promptly to the IRB.

470 Administration Building
701 20th Street South
205.934.3789
Fax 205.934.1301
irb@uab.edu

The University of
Alabama at Birmingham
Mailing Address:
AB 470
1530 3RD AVE S
BIRMINGHAM AL 35294-0104

GRADUATE SCHOOL
UNIVERSITY OF ALABAMA AT BIRMINGHAM
DISSERTATION APPROVAL FORM
DOCTOR OF PHILOSOPHY

Name of Candidate Han-Zhu Qian

Graduate Program Epidemiology

Title of Dissertation Association of Plasma Donation with Human Immunodeficiency Virus and Hepatitis C Virus Infections in Rural Shanxi Province, China

I certify that I have read this document and examined the student regarding its content. In my opinion, this dissertation conforms to acceptable standards of scholarly presentation and is adequate in scope and quality, and the attainments of this student are such that he may be recommended for the degree of Doctor of Philosophy.

Dissertation Committee:

Name		Signature
Sten H. Vermund	, **Chair**	
Eric Chamot		
Huey Chen		
Christopher Coffey		
Richard A. Kaslow		

Director of Graduate Program

Dean, UAB Graduate School

Date April 5, 2005