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Safety of the blood supply in a rural area of China

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Abstract

OBJECTIVE—To determine the sensitivity and specificity of tests for HBsAg, HCV, and syphilis conducted by laboratories of three blood collection organizations in a rural area of China.

METHODS—From October to December 2003, 1068 samples were collected from blood donors presenting to the three collection centers. All samples were tested twice using two different test kits for HBsAg, HCV, and syphilis. An aliquot was sent to the China National Center for Clinical Laboratories (NCCL) to confirm the local test results. Sensitivities and specificities of the three local blood centers/banks were calculated, using the results of the NCCL as the gold standard.

RESULTS—The sensitivity of the three blood collection center/banks ranged from 0% to 63.2% for HBsAg. For HCV, the sensitivity was 0%, and for syphilis, ranged from 0% to 85.7%. There were no HBsAg-positives in one of the blood center/banks, and no syphilis-positives in the other. Thus, sensitivity could not be measured for these tests in these two facilities. Combining all three tests, the overall sensitivity was 55.6%. The specificity was 100%.

CONCLUSION—The sensitivity of the local laboratories was inadequate, and could cause possible infection for an unacceptable number of blood recipients. Action needs to be taken to improve the quality of testing to ensure the safety of the rural blood supply.

Keywords

Blood safety; Hepatitis-B; hepatitis-C; Syphilis; Rural China

INTRODUCTION

Blood transfusions, while potentially life-saving, carry significant risk to the recipients, including transmission of infectious diseases such as HIV, HBV, HCV and syphilis. The epidemics of HIV and STDs have rapidly increased in China,^{1–5} HIV contaminated the plasma collection and supply in the 1990s.^{6–10} Until recently very few at risk persons have been tested for HIV and routine testing for HIV is often not done in rural areas.¹¹ The rapid rise in HIV & STD has not been paralleled by an equivalent rise in HIV testing rates, which

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remain low,^{12–17} Excluding contaminated blood from the blood supply by means of accurate and reliable testing, is therefore a critical step in ensuring the safety of blood particularly in rural areas.

In urban areas of China, good laboratory facilities are available, and there is a high enough demand for blood to sustain high quality laboratories. In rural areas, however, the safety of the blood supply is threatened by limited ability to sustain sophisticated laboratories with adequate quality management processes.^{13–17} In a rural area of Hebei, China, retesting of 5344 “safe” blood specimens collected by a city blood center showed false negative rates of 0.112% and 0.131% for HBV and HCV respectively¹². To assess the situation, we compared test results for three infectious diseases from laboratories in the rural blood banks in another rural area of China with those from a reference laboratory.

SUBJECTS AND METHODS

One city-level blood center and two county-level blood banks, one in proximity to the county site and one remote, were selected for study. Blood collection organizations are authorized by the Department of Health. The city blood center serves a population of 4.6 million, and collects about 25,000 units of blood annually; county blood bank A serves 950,000 persons, and collects about 4,000 units annually; and blood bank B serves 430,000 persons, and collects approximately 2,000 units annually. Donors included individual volunteers, groups of volunteers, and paid donors.

All donors presenting to the three collection sites October through December, 2003 were asked to participate in the study. If a donor consented, an additional 10 ml of blood was collected for supplementary testing. The study was approved by the institutional review boards of the University of California, Los Angeles and the Chinese Academy of Preventive Medicine.

All samples were tested for HCV, HBV and syphilis, in duplicate using two different test kits for each agent according to the routine procedures of the three blood collection organizations (Table 1). All tests were done by certified lab technicians. All testing procedures including results reading followed the instructions in the user manuals provided by test kits manufactures. All test kits were licensed and manufactured domestically (in China). A positive sample (or suspicious positive (this will need to be defined)) on either test was considered to be infected. An aliquot of each sample was transported to the China National Center for Clinical Laboratories (NCCL) for confirmation. NCCL is the only agency appointed by Chinese Ministry of Health and the “Chinese Blood Bank Regulations” that is authorized to make a final confirmatory lab test result. Serology tests for HBsAg, HCV, and syphilis were performed at the NCCL, using three different test kits (one imported, two domestic Table 1) for initial screening. Imported confirmatory tests were used to confirm all positive or suspicious (PIF comment; suspicious needs to be defined) samples in the screening tests (Table 1). All tests by NCCL were performed by senior technicians and in accordance with manufacturer’s instructions.

The study was reviewed and approved from the Institute Review Board (IRB) at the University of California at Los Angeles and the IRB at the National Center for AIDS/STD Control and Prevention, Chinese Center for Disease Control and Prevention.

RESULTS

Samples were collected from 1068 donors. The city blood center collected 650 samples, county blood bank A, 200 samples, and county blood bank B, 218 samples. The refusal rates were 5–10% in the city blood center, 0.5% in county blood bank A, and 1.4% in county

blood bank B. Table 2 presents the demographic characteristics of the donors at the three centers. Donors at the city blood bank were younger than those at the county blood banks. Table 3 compares test results for the three rural blood collection organizations and NCCL, and Table 4 presents the sensitivity and specificity of the tests performed by the three local centers, using the NCCL test results as the gold standard.

HBsAg

All 12 HBsAg-positives identified by the city blood center repeated positive. (Table 2). However, seven of the reported negatives were actually positive according to the NCCL laboratory; the sensitivity was therefore 63.2% (Table 3). In county blood bank A, there were no HBsAg-positive samples; therefore, sensitivity could not be evaluated. In county blood bank B, two of the positive samples repeated positive, but there were two false-negative tests; thus, the sensitivity was only 50% (Table 4). The specificity in the city blood center and the two county blood banks was 100%.

HCV

The city blood center failed to identify the single positive sample identified by the NCCL laboratory. County blood bank A had no HCV-positive samples, and county blood bank B failed to identify the two positive samples. The specificity in the city blood center and the two county blood banks was 100%.

Syphilis

The city blood center identified six of seven positive samples; thus, sensitivity was 85.7%. County blood bank A missed all three positive samples (sensitivity=0%), and county blood bank B had no positive samples. The specificity was 100% in all three facilities.

Composite sensitivity and specificity

Among the 650 samples from the city blood center, 27 were confirmed as positive, nine of which had not been detected, rendering a sensitivity of 66.7% (Table 5). The specificity was 100%.

Among the 200 samples from county blood bank A, three were confirmed as positive, all of which were undetected (sensitivity=0%). There were no false-positive samples; therefore, specificity was 100%.

Among the 218 samples from county blood bank B, six were confirmed as positive, among which four had not been detected (sensitivity=33.3%). The specificity was 100%.

The composite sensitivity was 55.6% (only 20 of the 36 tests positive at the NCCL were identified by the local laboratories), and the specificity was 100%. Overall, 14 of every 1000 (1.4%) blood units labeled by the city blood center as pathogen-free would be expected to be contaminated with one of these three agents, as would 15 of 1000 (1.5%) from county blood bank A and 19/1000 (1.9%) from county blood bank B.

DISCUSSION

Exclusion of infectious donations from the blood supply is primarily dependent on accurate and reliable testing for transfusion-transmitted pathogens. Our study was designed to detect differences in donor test results between three identified blood centers and the laboratory designated as the authoritative laboratory for donor test confirmation by the Chinese Ministry of Health. Using the NCCLS laboratory as the standard for testing, our study reveals that there were serious problems with detecting HBsAg, HCV antibodies, and

syphilis antibodies in the city blood center and in the two county-level blood banks. Retesting the city blood center samples identified the highest proportion of contaminated samples, 66.7%, which means that they would have labeled almost one-third of the infected blood units as pathogen-free. County blood bank B would have labeled two-thirds of the contaminated units as pathogen-free, and county blood bank A, all of the contaminated units as pathogen-free. Because the prevalence of pathogens was low in the study populations, the calculation of the sensitivities was unstable and the confidence limits for sensitivity and specificity were wide in some instances.

Accuracy and reliability of test results are a function of the sensitivity and specificity of test kits, quality of specimen, competency of testing personnel, and adherence to good laboratory practices. Our study was not designed to identify which of these factors was responsible for the discrepant results. We cannot say whether the apparently low sensitivity in the rural laboratories was due to the poor quality of test kits themselves, or due to test procedures by the lab technicians, or both. It is also possible, but less likely, that the results of the NCCLS laboratory, which we used as the “gold standard” were incorrect.

Our results do indicate that reliability of donor infectious disease screening performed at the three collection centers we studied is uncertain, and that there is a need to assess to what degree this may be true throughout similar rural communities. In China, urban blood collection centers are generally staffed with trained laboratory professionals and are expected to have quality assurance measures in place. However, it is hard to recruit highly trained professionals to work in the rural areas, and quality assurance may be an unfamiliar concept.

As the prevalence of transfusion transmitted disease increases in the population, the threat to the blood supply increases. Measures to standardize and improve donor infectious disease screening are urgently needed. These measures should include validation of test kits, better training, implementation of standardized quality control and quality assurance procedures, and periodic recertification of laboratory technicians. Most of these recommendations are already included in the official blood collection regulations^{18–21}, but are not uniformly enforced, especially in rural areas.

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References

1. Abrams HK. The resurgence of sexually transmitted disease in China. *J Public Health Policy*. 2001; 22(4):429–40. [PubMed: 11787308]
2. Beyrer C. Hidden epidemic of sexually transmitted diseases in China: crisis and opportunity. *JAMA*. 2003; 289(10):1303–5. [PubMed: 12633193]
3. Lin CC, Gao X, Chen XS, Chen Q, Cohen MS. China's syphilis epidemic: a systematic review of seroprevalence studies. *Sex Transm Dis*. 2006; 33(12):726–36. [PubMed: 16755273]
4. Wu Z, Rou KM, Cui HX. The HIV/AIDS epidemic in China: history, current strategies and future challenges. *AIDS Educ Prevent*. 2004; 16 (Suppl A):7–17.

5. Ministry of Health of China, UNAIDS, and WHO. 2005 Update on the HIV/AIDS Epidemic and Response in China. 2006
6. Wu Z, Rou K, Detels R. Prevalence of HIV infection among former commercial plasma donors in rural eastern China. *Hlth Policy Planning*. 2001; 16(1):41–6.
7. Volkow P, del Rio C. Paid donation and plasma trade: unrecognized forces that drive the AIDS epidemic in developing countries. *Intl J STD AIDS*. 2005; 16:5–8.
8. Qian HZ, Yang ZM, Shi XM, et al. Hepatitis C virus infection in former commercial plasma/blood donors in rural Shanxi Province, China. *The China Integrated Program for Research on AIDS*. *J Infect Dis*. 2005; 192:1694–700. [PubMed: 16235166]
9. Zaller N, Nelson KE, Ness P, et al. Demographic characteristics and risks for transfusion-transmissible infection among blood donors in Xinjiang autonomous region, People's Republic of China. *Transfusion*. 2006 Feb; 46(2):265–71. [PubMed: 16441605]
10. Ji GP, Detels R, Wu Z, et al. Correlates of HIV infection among former blood/plasma donors in rural China. *AIDS*. 2006; 20:585–91. [PubMed: 16470123]
11. Wu Z, Sun XH, Sullivan S, Detels R. Public health. HIV testing in China *Science*. 2006; 312:1475–6.
12. Li BS, Tan P, Yang BC, et al. An analysis of the infectiousness of blood specimens in blood banks. *Hebei Med J*. 2001; 10:741–2.
13. Shan H, Wang JX, Ren FR, et al. Blood banking in China. *Lancet*. 2002; 360:1770–5. [PubMed: 12480443]
14. Lu YF, Yin P, Liu TY. Analysis on quality control of blood in blood banks in a five-year program in Hunan province. *Chin J Epidemiol*. 2003; 24:574–6.
15. Cohen J. An unsafe practice turned blood donors into victims. *Science*. 2004; 304:1438–9. [PubMed: 15178781]
16. Dodd RY. Plasma collection and donor safety in rural China. *J Infect Dis*. 2005; 192:1681–2. [PubMed: 16235163]
17. Shang G, Seed CR, Wang F, Nie D, Farrugia A. Residual risk of transfusion-transmitted viral infections in Shenzhen, China, 2001 through 2004. *Transfusion*. 2007; 47(3):529–39. [PubMed: 17319836]
18. Department of Health Services. Regulations on clinical use of whole blood and blood components in medical settings. Beijing: Chinese Ministry of Health; January 5. 1999
19. Department of Health Services. Clinical technical guidelines on transfusion. Beijing: Chinese Ministry of Health; June 2. 2000
20. Regulations of Blood Banks. Beijing: Chinese Ministry of Health; November 17. 2005
21. Department of Health Services. Principles for designing agencies for blood collection and supply. Beijing: Chinese Ministry of Health; December 16. 2005

Test methods and test kits used by China National Center for Clinical Laboratories (NCCL) and the three blood center/banks

Table 1

Organization	Serologic indicator	Screening [#]		Confirmation [*] /Screening [*]	
		Method	Test kits (company)	Method	Test kits (company)
NCCL	HBsAg	ELISA	Xinchuang (Xiamen Xinchuang) Wantai (Beijing Wantai)	Neutralization assay	Ortho (Johnson & Johnson)
	anti-HCV	ELISA	Ortho (Johnson & Johnson)	RIBA	Ortho (Johnson & Johnson)
			Wantai (Beijing Wantai)		
			Xinchuang (Xiamen Xinchuang)		
	anti-syphilis	ELISA	Ortho (Johnson & Johnson)	TPPA	Fuji (Fuji Co., Ltd)
			GBI (Beijing GBI)		
City blood center	HBsAg	ELISA	Xinchuang (Xiamen Xinchuang)	ELISA	Pusheng (Tianjin Pusheng)
			Huamei (Luoyang Huamei)		
	anti-HCV	ELISA	GBI (Beijing GBI)	ELISA	Lili (Henan Lili)
			Xinchuang (Xiamen Xinchuang)		
	anti-syphilis	ELISA	Huamei (Luoyang Huamei)	ELISA	Pusheng (Tianjin Pusheng)
			Huamei (Luoyang Huamei)		
County blood bank A	HBsAg	ELISA	Jinhao (Beijing Jinhao)	ELISA	GBI (Beijing GBI)
	anti-HCV	ELISA	Huamei (Luoyang Huamei)	ELISA	Xinchuang (Xiamen Xinchuang)
	anti-syphilis	RPR	Rongsheng (Shanghai Rongsheng)	RPR	Xinchuang (Xiamen Xinchuang)
County blood bank B	HBsAg	ELISA	Xinchuang (Xiamen Xinchuang)	ELISA	Kehua (Shanghai Kehua)
	anti-HCV	ELISA	Huamei (Luoyang Huamei)	ELISA	Huamei (Luoyang Huamei)
	anti-syphilis	TRUST	Rongsheng (Shanghai Rongsheng)	RPR	Huamei (Luoyang Huamei)

[#] NCCL used the methods and test kits to do three times of screening, and the blood center/banks used the methods and test kits to do the first screening.

^{*} NCCL used the methods and test kits to do confirmation, and the blood center/banks used the methods and test kits to do the second screening.

Table 2

Basic demographic characteristics of the blood donors in the three rural blood center/banks

		City blood bank n(%)	County blood bank A n(%)	County blood bank B n(%)
		(N=650)	(N=200)	(N=221 [*])
Gender	Male	312(48.0)	107(53.5)	111(50.2)
	Female	338(52.0)	93(46.5)	110(49.8)
Average age		28.5 [#]	41.6	37.5
Type of donation	Paid	164(25.2)	191 (95.5)	128(57.9)
	voluntary	486(74.8)	9(4.5)	93(42.1)

^{*} Three people were not collected blood samples. We only had 218 samples from county blood bank B.

[#] Many blood donors were college students, so the average age was smaller than the other two blood banks.

Table 3
Comparison by category of test results between blood center/banks and NCCL, China, 2003

NCCL												
	HBsAg			Total			HCV			Syphilis		
	+	-		+	-		+	-		+	-	Total
City blood center	+	12	0	12	0	0	0	0	0	6	0	6
	-	7	631	638	1	649	650	1	643	1	643	644
	sum	19	631	650	1	649	650	1	643	7	643	650
County blood bank A	+	0	0	0	0	0	0	0	0	0	0	0
	-	0	200	200	0	200	200	3	197	3	197	200
	sum	0	200	200	0	200	200	3	197	3	197	200
County blood bank B	+	2	0	2	0	0	0	0	0	0	0	0
	-	2	214	216	2	216	218	0	218	0	218	218
	sum	4	214	218	2	216	218	0	218	0	218	218

Table 4

Assessment indicators of test results by labs for three blood center/banks in rural China, 2003

	indicators	HBsAg (95% CL [*])	anti-HCV (95% CL)	anti-syphilis (95% CL)
City blood center	Sensitivity	0.632 (0.386, 0.828)	0.000 (0, 0.945)	0.857 (0.420, 0.992)
	Specificity	1.000 (0.992, 1.000)	1.000 (0.993, 1.000)	1.000 (0.993, 1.000)
County blood bank A	Sensitivity	NA	NA	0.000 (0, 0.690)
	Specificity	1.000 (0.977, 1.000)	1.000 (0.977, 1.000)	1.000 (0.976, 1.000)
County blood bank B	Sensitivity	0.500 (0.092, 0.908)	0.000 (0, 0.802)	NA
	Specificity	1.000 (0.978, 1.000)	1.000 (0.978, 1.000)	1.000 (0.978, 1.000)

*
CL: confidence limits.

Table 5

Assessment indicators of composite test results by three blood center/banks in rural China, 2003

Indicators	City blood center (95% CL)	County blood bank A (95% CL)	County blood bank B (95% CL)	All three blood center/banks (95% CL)
Sensitivity	0.667 (0.460, 0.828)	0.000 (0, 0.690)	0.333 (0.060, 0.759)	0.556 (0.383, 0.717)
Specificity	1.000 (0.992, 1.000)	1.000 (0.976, 1.000)	1.000 (0.978, 1.000)	1.000 (0.995, 1.000)
Predictive Value of Positive	1.000	NA	1.000	1.000