Prevalences, Genotypes, and Risk Factors for HIV Transmission in South America

Silvia M. Montano, MD, MPH, Jose L. Sanchez, MD, MPH,*† Alberto Laguna-Torres, MD, MTMH,* Paloma Cuchi, MD,‡ Maria M. Avila, MD, PhD,§ Mercedes Weissenbacher, MD,§ Margarita Serra, MD,§ Jose Viñoles, MD,§ Jose C. Russi, MD,§ Nicolas Aguayo, MD,§ Adolfo H. Galeano, MD,§ Alberto Gianella, MD,§ Ronald Andrade, MD,§ Anabella Arredondo, MD,§ Eugenio Ramirez, PhD,§ Maria E. Acosta, MD,§ Aracely Alava, PhD,§ Orlando Montoya, BS,§ Angel Guevara, PhD,§ Hugo Manrique, MD,§ Jorge L. Sanchez, MD, MPH,§ Javier R. Lama, MD, MPH,§ Fernando de la Hoz, MD,§ Gloria I. Sanchez, PhD,§ Claudia Ayala,§ Maria E. Pacheco, PhD,§ Gladys Carrion, BS,* Gloria Chauca, BS,* Juan J. Perez, BS,* Monica Negrete, MD, MPH,* Kevin L. Russell, MD, MTMH,* Christian T. Bautista, MSc,*† James G. Olson, PhD,* Douglas M. Watts, PhD,‖ Deborah L. Birx, MD,† and Jean K. Carr, PhD, MSH† for the South American HIV Molecular Surveillance Working Group*

Summary: HIV cross-sectional studies were conducted among high-risk populations in 9 countries of South America. Enzyme-linked immunosorbent assay screening and Western blot confirmatory testing were performed, and *env* heteroduplex mobility assay genotyping and DNA sequencing were performed on a subset of HIV-positive subjects. HIV prevalences were highest among men who have sex with men (MSM; 2.0%–27.8%) and were found to be associated with multiple partners, noninjection drug use (non-IDU), and sexually transmitted infections (STIs). By comparison, much lower prevalences were noted among female commercial sex workers (FCSWs; 0%–6.3%) and were associated mainly with a prior IDU and STI history. *Env* subtype B predominated among MSM throughout the region (more than 90% of strains), whereas *env* subtype F predominated among FCSWs in Argentina and male commercial sex workers in Uruguay (more than 50% of strains). A renewed effort in controlling STIs, especially among MSM groups, could significantly lessen the impact of the HIV epidemic in South America.

Key Words: HIV, prevalence, risk factors, molecular epidemiology, genotypes, surveillance, commercial sex workers

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From the *US Naval Medical Research Center Detachment–Lima, Peru; †US Military HIV Research Program at the Walter Reed Army Institute of Research and Henry M. Jackson Foundation, Rockville, MD; ‡Pan-American Health Organization, Washington, DC; §South American HIV Molecular Surveillance Working Group; and ‖University of Texas Medical Branch at Galveston, Galveston, TX.

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Reprints: Jose L. Sanchez, US Military HIV Research Program, Walter Reed Army Institute of Research, 1 Taft Court, Suite 250, Rockville, MD 20850 (e-mail: jsanchez@hivresearch.org).

The pandemic caused by HIV constitutes the largest viral epidemic since the influenza pandemic of 1917 through 1918.[1] Almost 38 million persons are living with HIV worldwide,[2] and the virus' complex genetic variability and different modes of transmission have contributed greatly to its rapid spread. The dynamic nature of the HIV epidemic requires the maintenance of a continued, systematic, large-scale surveillance effort to assess the importance of new and divergent strains (including recombinants) of HIV.[3]

HIV prevalence among female commercial sex workers (FCSWs) varies by geographic region; higher infection frequencies have been reported in sub-Saharan Africa (0.2%–60.5%), followed by South and Southeast Asia (0.0%–26.0%).[4] In Latin America and the Caribbean, lower infection prevalences have been documented (0.0%–14.0%)[4] and HIV transmission among other high-risk groups such as men who have sex with men (MSM) and injection drug users seems to prevail. The status of the HIV epidemic among MSM in Latin America and the Caribbean has been reviewed elsewhere.[5] Additionally, 2 recent studies have just been published by our group,[6,7] and updated data among FCSWs and MSM in the region have been presented elsewhere.[8–10]

The geographic and temporal surveillance of the distinct genotypes of HIV also facilitates the definition of prevention and control strategies.[3,11] As an illustration of the importance of molecular surveillance of HIV, rapid dissemination of new strains among at-risk groups in Thailand has been documented

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during the past decade,[12,13] and, worldwide, up to 9 subtypes and 16 circulating recombinant forms (CRFs) have been identified.[14] In South America, 5 distinct subtypes (A, B, C, D, and F)[15–22] and 2 CRFs[23–26] have been described, including CRF12_BF, a recombinant form that seems to be unique to South America.[24]

We present a summary of multiple cross-sectional studies conducted among FCSWs and MSM in 9 countries of South America, including an analysis of the genetic variability among HIV-1 strains.

MATERIALS AND METHODS

Study Population

Cross-sectional studies among at-risk groups were performed in 42 cities of 9 South American countries. Additionally, antenatal clinic (ANC), tuberculosis (TB), and HIV-positive patients were sampled in certain locations such as Peru.[27] These studies were conducted by scientists from local country's Ministry of Health (MOH) national AIDS control programs, AIDS-supporting nongovernmental organizations (NGOs) in collaboration and coordination with the Pan-American Health Organization (PAHO), US Naval Medical Research Center Detachment–Lima (NMRCD–Lima), Walter Reed Army Institute of Research (WRAIR), and Henry M. Jackson Foundation (HJF), as described elsewhere.[7,9,25] Central funding and laboratory genotyping support were provided by the US Military HIV Research Program (USMHRP) at the WRAIR. All study protocols were approved by the US Navy and Army Human Use and Institutional Review Boards and by local ethical review boards.

Enrollment and Data Collection Procedures

Potential study subjects were invited to participate by trained social workers and peer risk group counselors. FCSWs were contacted at brothels, saunas, massage houses, parks, and streets; MSM were contacted at public and private venues and meeting locations (discotheques and bars); and street-based male commercial sex workers were recruited in Montevideo, Uruguay. Subjects were recruited after being given an explanation of study procedures, risks, and benefits of participation. All subjects were adults (eg, at least 18 years of age) and provided written informed consent. Pre- and post-test counseling as well as subsequent referral to appropriate medical authorities was provided. No records of potential versus actual participants were collected in these studies; therefore, no assessment of completeness and representativeness of FCSW and MSM participation could be achieved.

Country-specific questionnaires were developed and administered in face-to-face interviews. Demographic and epidemiologic data were collected, which included weekly number and type of sexual partners, history of prior sexually transmitted infections (STIs), sexual contact with foreigners, use of condoms, history of sex for money, alcohol use, injection drug use (IDU), and prior history of blood transfusions.

Blood Sampling and HIV Testing Procedures

A blood sample (4–7 mL) was obtained from freshly spun EDTA-containing tubes. Peripheral blood mononuclear cells (PBMCs) were separated by density gradient and stored at −20°C to −70°C; if this was not possible, blood was stored on filter paper cards. Plasma was later processed within 2 weeks for serologic HIV-1 reactivity testing. Initial testing was performed with the Genetic Systems rLAV enzyme-linked immunosorbent assay (ELISA; Bio-Rad, Hercules, CA); confirmation of infection was attained with Cambridge Biotech Western blot (WB) test kits (Calypte Biomedical, Alameda, CA). Only samples that were repeatedly reactive by ELISA and that showed a WB banding pattern with at least 2 or more specific antigens (p24, gp41, gp120, or gp160) present were coded as HIV-positive.

Genotyping Procedures

DNA was extracted from PBMCs, blood spots, or cocultivation of fresh whole blood samples using the QIAamp blood extraction kit (QIAgen, Valencia, CA) as described elsewhere.[28] By means of performance of the envelope-based heteroduplex mobility assay (*env* HMA), polymerase chain reaction (PCR) amplification of C2 through V4 of *env* was conducted as described by Delwart et al,[29] and the amplified products were hybridized to known reference subtype plasmids and electrophoresed in polyacrylamide. Rapid mobility of the homoduplex assay compared with the heteroduplex assay revealed the *env* subtype. For genotyping testing, all samples were selected at random.

Statistical Analysis

The χ^2 or Fisher exact test was applied to compare differences in categoric variables; the Mann-Whitney U or Kruskal-Wallis H test was used for comparison of continuous variables. Age was categorized into 4 groups (18–20 years, 21–30 years, 31–40 years, and older than 40 years) to evaluate an increasing HIV prevalence with age by the χ^2 test for trend. Risk factors associated with HIV infection were expressed as odds ratios (ORs); age and country adjustments were estimated in univariate and multiple logistic regression analyses as well as associated 95% confidence intervals (95% CIs). Risk factors found to be at least marginally significant in univariate analysis ($P \leq 0.15$) were entered in a forward stepwise selection multivariate logistic regression model to identify independent risk factors associated with HIV-1 infection. Separate risk factor comparisons were conducted for countries of the Andean region and Southern Cone region. Data analyses were performed using SPSS version 10 (SPSS Corporation, Chicago, IL) and SAS version 8.0 (SAS Institute, Cary, NC).

RESULTS

A total of 42,358 individuals were surveyed between 1995 and 2002; these included 13,600 FCSWs, 13,847 MSM, 13,462 ANC patients, 51 ANC partners, and 489 TB patients. Additionally, 946 already identified HIV-positive individuals were included for purposes of genotyping. HIV prevalences among FCSWs were found to be much lower (1.2% overall, range: 0%–6.3%) than among MSM (12.3% overall, range: 2.0%–27.8%; $P < 0.01$). Higher prevalences were detected in urban areas (Table 1).

TABLE 1. HIV-1 Prevalences in South America Among Risk Groups (FCSWs, MSM, and MCSWs), 1999–2002

				Total Enrolled	HIV-Positive	
Risk Group	**Country**	**Location**	**Period**	**(n)**	**(n)**	**(%)**
FCSW	Venezuela	Isla Margarita	2002	652	0	(0.0)
	Colombia	Bogota	2001–2002	514	4	(0.8)
	Ecuador	Quito	2000–2001	200	1	(0.5)
		Guayaquil	**2000–2001**	**1047**	**22**	**(2.1)**
	Peru	Lima (urban)	1999–2000	3374	53	(1.6)
		Provinces (rural)	1999–2000	4930	31	(0.6)
	Chile	Santiago	2000	626	0	(0.0)
	Bolivia	Santa Cruz	2001	195	1	(0.5)
		Border cities with Argentina (3)	2002	77	0	(0.0)
	Paraguay	**Asuncion and 4 other cities**	**2002**	**743**	**19**	**(2.6)**
	Uruguay	Montevideo	2000	308	1	(0.3)
		Border cities with Brazil (5)	2002	308	4	(1.3)
	Argentina	**Buenos Aires**	**2000–2001**	**304**	**19**	**(6.3)**
		Provinces (7 cities)	2001–2002	322	9	(2.8)
	Total			13,600	164	(1.2)
MSM	Colombia	**Bogota**	**2002**	**660**	**130**	**(19.7)**
	Ecuador	Quito	1999–2001	263	38	(14.5)
		Guayaquil	**1999–2001**	**227**	**63**	**(27.8)**
		Other city ports (4)	2001–2002	142	4	(2.8)
	Peru	Lima (urban)	1999–2000	7041	968	(13.7)
		Provinces (rural)	1999–2000	3898	236	(6.1)
	Bolivia	La Paz	1999–2001	48	7	(14.6)
		Santa Cruz	**2001–2002**	**186**	**44**	**(23.7)**
		Other cities (3)	2002	52	8	(15.4)
	Paraguay	Asuncion	2002	92	12	(13.0)
	Uruguay	**Montevideo MCSW**	**1999–2001**	**317**	**69**	**(21.8)**
		Border cities with Brazil (5)	2001–2002	102	2	(2.0)
	Argentina	Buenos Aires	2000–2001	742	114	(15.4)
		Provinces (7 cities)	2001–2002	77	5	(6.5)
	Total			13,847	1700	(12.3)

Statistically significant variables ($P < 0.05$) are illustrated in boldface.
MCSWs indicates male commercial sex workers.

Among FCSWs, HIV prevalence increased with age ($P < 0.05$) and higher prevalences were noted in the cities of Buenos Aires (6.3%), Asuncion and border cities with Brazil (2.6%), and Guayaquil (2.1%). HIV-positive MSM were found to be significantly older than HIV-negative MSM (median ages: 28 vs. 24 years; $P < 0.001$), and higher HIV prevalences were found in the cities of Guayaquil (27.8%), Santa Cruz (23.7%), Montevideo (21.8%), and Bogota (19.7%).

Risk Factors

Among FCSWs, ≥4 sexual partners per week, a prior STI history, prior drug use of any kind, use of marihuana or heroin, a history of IDU, and a history of alcohol use were found to be associated with HIV infection after adjusting by age and country. In comparison, HIV-infected MSM reported that ≥2 sexual partners per week, a prior STI history, sexual contact with foreigners, prior drug use of any kind, use of marihuana or cocaine, a non-IDU history, and a history of alcohol use were associated with HIV infection (Table 2).

For FCSWs, independent risk factors for HIV infection included a prior STI history (OR = 3.4, 95% CI: 2.2–5.3; $P < 0.001$), a non-IDU use history (OR = 2.2, 95% CI: 1.0–5.0; $P = 0.049$), and a history of IDU (OR = 20.6, 95% CI: 2.0–215.1; $P = 0.011$). By comparison, for MSM, risk factors included a prior STI history (OR = 2.3, 95% CI: 2.0–2.5; $P < 0.001$), a greater number of sexual partners per week (OR = 1.4, 95% CI: 1.1–1.8; $P = 0.003$ for 2 or 3 partners and OR = 2.0, 95% CI: 1.6–2.3; $P < 0.001$ for ≥4 partners), sexual contact with foreigners (OR = 1.6, 95% CI: 1.4–1.9; $P < 0.001$), and use of cocaine (OR = 1.8, 95% CI: 1.3–2.3; $P < 0.001$).

To seek a better understanding of risk factors for HIV infection among MSM in the region, separate analyses were done for countries of the Andean region (Venezuela,

TABLE 2. Logistic Regression Analysis of Risk Factors Associated With HIV-1 Infection Among FCSWs and MSM Groups in South America, 1999–2002

	FCSW			MSM		
Risk Factor	**HIV % (n)***	**AOR**	**(95% CI)**	**HIV % (n)***	**AOR**	**(95% CI)**
No, sexual partners per week						
2 or 3 (none or 1)	1.3 (1669)	1.6	(0.9–2.9)	16.4 (628)	**1.4**	**(1.1–1.7)**
4 or more (none or 1)	1.4 (6663)	**1.9**	**(1.2–2.9)**	22.7 (915)	**2.3**	**(1.9–2.7)**
Sexually transmitted infection history (no)	3.9 (719)	**3.5**	**(2.2–5.5)**	19.7 (3199)	**2.2**	**(2.0–2.5)**
Sexual contact with foreigners (no)	1.1 (4002)	1.0	(0.7–1.4)	21.0 (1427)	**2.0**	**(1.7–2.3)**
Use of drugs (no)	3.6 (275)	**3.2**	**(1.7–6.3)**	21.7 (727)	**1.9**	**(1.6–2.4)**
Use of marijuana (no)	3.9 (154)	**3.3**	**(1.4–7.7)**	18.2 (555)	**1.5**	**(1.1–1.8)**
Use of heroin (no)	13.3 (15)	11.3	(2.5–51.0)	13.0 (23)	0.9	(0.3–3.0)
Use of cocaine (no)	3.0 (134)	2.3	(0.8–6.3)	27.2 (316)	**2.5**	**(1.9–3.2)**
Highest drug use profile						
Non-IDU (none)	2.7 (261)	2.2	(0.9–4.7)	23.3 (604)	**2.1**	**(1.7–2.6)**
IDU (none)	33.3 (6)	38.8	(7.0–215.8)	23.3 (30)	2.2	(0.9–5.2)
Use of alcohol (no)	2.0 (1782)	**1.8**	**(1.2–2.6)**	17.0 (2022)	**1.5**	**(1.3–1.7)**
Blood transfusion history (no)	2.6 (379)	1.9	(0.9–3.7)	15.7 (134)	0.9	(0.6–1.6)

*HIV% (n) describes the HIV prevalence of the category and, in parentheses, the number of participants.
Statistically significant variables are illustrated in boldface.
Categories in parentheses describe the reference category for odds calculations.
AOR indicates adjusted odds ratio by age (y) and country.

Colombia, Ecuador, Peru, and Bolivia) and Southern Cone region (Chile, Argentina, Uruguay, and Paraguay). Multiple partners per week, a prior STI history, sexual contact with foreigners, prior drug use of any kind, cocaine use, and a non-IDU history were associated with HIV infection in the Andean countries. The same significant risk factors were found to be associated with HIV infection in the Southern Cone countries, with the exception of number of sexual partners per week, where only 4 or more sexual partners was significant (Table 3). Given the low number of HIV-infected FCSWs, separate region analyses could not be performed.

Risk factors associated with subtype B infection were found to be similar to those associated with risk of F infection, although the small number of F infections decreased the power of this analysis (Table 4). There was a significant difference in the risk associated with IDU history, however. A 65-fold increase in risk for subtype B infection was found to be associated with a history of IDU only among FCSWs. Among MSM, sexual contact with foreigners was associated with a 2-fold increased risk for subtype B and an 8-fold increased risk for subtype F. The risk of infection for injection drug users was 35-fold for subtype F. Among FCSWs and MSM, there was no risk associated with a prior STI history for infection with subtype F, although there was, in both groups, for subtype B. Additionally, among MSM but not in FCSWs, there was an increased risk of acquiring B and F strains associated with 4 or more sexual partners per week, sexual contact with foreigners, and IDU.

In general, a history of IDU and a prior STI history were the 2 major risk factors among FCSWs, and they were associated with an increased prevalence of infection with

TABLE 3. Logistic Regression Analysis of Risk Factors Associated With HIV-1 Infection Among MSM by Region in South America, 1999–2002

	Andean Region		Southern Cone Region	
Risk Factor	**AOR**	**(95% CI)**	**AOR**	**(95% CI)**
No, sexual partners per week				
2 or 3 (none or 1)	**1.7**	**(1.3–2.1)**	1.4	(0.8–2.5)
4 or more (none or 1)	**3.0**	**(2.4–3.8)**	**2.4**	**(1.4–4.0)**
Sexually transmitted infection history (no)	**2.3**	**(2.0–2.6)**	**1.6**	**(1.1–2.4)**
Sexual contact with foreigners (no)	**1.9**	**(1.6–2.3)**	**1.6**	**(1.2–2.2)**
Use of drugs (no)	**1.4**	**(1.0–1.8)**	**1.9**	**(1.4–2.8)**
Use of marijuana (no)	1.1	(0.8–1.5)	1.2	(0.8–1.8)
Use of heroin (no)	0.9	(0.3–3.0)	NA	—
Use of cocaine (no)	**1.7**	**(1.2–2.5)**	**2.3**	**(1.6–3.6)**
Highest drug use profile				
Non-IDU (none)	**1.6**	**(1.2–2.2)**	**1.9**	**(1.4–2.8)**
IDU (none)	1.3	(0.4–4.0)	2.9	(0.7–11.4)
Use of alcohol (no)	1.0	(0.7–1.3)	1.0	(0.8–1.4)
Blood transfusion history (no)	0.7	(0.4–1.4)	1.1	(0.5–2.4)

Statistically significant variables are illustrated in boldface.
Categories in parentheses describe the reference category for odds calculations.
NA, not applicable; AOR, adjusted odds ratio by age (y) and country; Andean region indicates Venezuela, Colombia, Ecuador, Peru, and Bolivia; Southern Cone Region indicates Chile, Argentina, Uruguay, and Paraguay.

TABLE 4. Logistic Regression Analysis of Risk Factors Associated With HIV-1 B and F *env* Subtype Seropositivity Among FCSWs and MSM in South America, 1999–2002

	FCSW				MSM			
	B Subtype (n = 51)		F Subtype (n = 15)		B Subtype (n = 590)		F Subtype (n = 51)	
Risk Factors	AOR	(95% CI)	AOR	(95% CI)	AOR	(95% CI)	AOR	(95% CI)
No, sexual partners per week								
2 or 3 (none or 1)	1.9	(0.8–4.3)	0.1	(0.1–3.1)	1.4	(0.9–1.9)	3.1	(0.9–10.7)
4 or more (none or 1)	1.0	(0.5–2.0)	6.0	(0.7–49.7)	**2.1**	**(1.6–2.8)**	**23.0**	**(12.1–43.6)**
Sexually transmitted infection history (no)	**2.9**	**(1.2–7.0)**	0.1	(0.1–1.5)	**2.7**	**(2.2–3.2)**	0.5	(0.2–1.2)
Sexual contact with foreigners (no)	0.7	(0.4–1.4)	0.9	(0.2–4.5)	**1.8**	**(1.4–2.2)**	**8.0**	**(4.4–14.7)**
Use of drugs (no)	**5.1**	**(1.9–13.3)**	**10.5**	**(1.9–59.8)**	**2.2**	**(1.7–2.9)**	**11.2**	**(5.7–22.2)**
Use of marijuana (no)	3.5	(0.8–14.9)	**10.2**	**(1.1–93.3)**	**1.7**	**(1.2–2.3)**	**6.2**	**(2.6–14.9)**
Use of heroin (no)	**18.7**	**(2.4–150.1)**	0.1	(0.1–6.9)	1.8	(0.5–6.2)	0.1	(0.1–6.7)
Use of cocaine (no)	**6.0**	**(1.8–19.9)**	6.6	(0.7–58.7)	**2.6**	**(1.9–3.7)**	**10.9**	**(5.1–23.7)**
Highest drug use profile								
Non-IDU (none)	**4.2**	**(1.5–12.1)**	**11.8**	**(2.1–67.2)**	**2.2**	**(1.6–2.9)**	**12.1**	**(6.0–24.5)**
IDU (none)	**65.0**	**(7.0–600.0)**	0.1	(0.1–3.3)	2.9	(0.9–8.5)	**34.8**	**(7.7–156.5)**
Use of alcohol (no)	1.6	(0.8–3.3)	0.1	(0.1–3.5)	**2.3**	**(1.8–2.9)**	**7.5**	**(3.9–14.5)**
Blood transfusion history (no)	**5.2**	**(2.2–12.0)**	1.2	(0.1–10.2)	1.6	(0.9–2.7)	1.5	(0.2–11.1)

The reference group was the HIV-negative group for B and F *env* subtypes.
Statistically significant variables are illustrated in boldface.
Categories in parentheses describe the reference category for odds calculations.
AOR indicates adjusted odds ratio by age (y) and country.

subtype B but not subtype F strains. Among MSM, conversely, an IDU history seems to be associated with an increased HIV prevalence of infection for subtype B and F strains, but the risk for subtype F is 10 times higher than the risk for subtype B.

Genotyping

A total of 1496 HIV-positive samples were collected and genotyped by HMA (Table 5). *Env* subtype B strains were found to predominate in the Andean region countries where 93% to 100% of strains were of subtype B. By comparison, a greater proportion of F subtype strains were found in the Southern Cone countries of Argentina (52%), Uruguay (53%), and Paraguay (14%). Other non-B subtypes (C subtypes) were also found in a small number of subjects in Ecuador, Peru, Argentina, and Uruguay, including 2 Uruguayan male commercial sex workers who lived and worked in cities along the border with Brazil.

TABLE 5. HMA Subtype Distribution by Country in South America, 1995–2002

		HMA Subtype					
		B		F		Others (C)	
Country	Genotyped Samples (n)	(n)	(%)	(n)	(%)	(n)	(%)
Venezuela	2	2	(100)	—	—	—	—
Colombia	237	237	(100)	—	—	—	—
Ecuador	238	233	(97.9)	2	(0.8)	3	(1.3)
Peru	484	475	(98.1)	8	(1.7)	1	(0.2)
Bolivia	128	119	(93.0)	9	(7.0)	—	—
Chile	8	8	(100)	—	—	—	—
Argentina	314	151	(48.1)	162	(51.6)	1	(0.3)
Uruguay	64	28	(43.8)	34	(53.1)	2	(3.1)
Paraguay	21	18	(85.7)	3	(14.3)	—	—
Total	1496	1271	(85.0)	218	(14.6)	7	(0.5)

DISCUSSION

The updated HIV risk factor information presented in this report provides us with a better understanding of the status of the HIV epidemic in South America. The implementation of a standardized systematic genetic surveillance effort in the region has also enabled us to assess HIV genetic variability more accurately as the epidemic changes. Such variability is a central feature of HIV, and the extensive genetic heterogeneity can greatly influence the development of adequate diagnosis, treatment, and vaccine prevention tools against it.[3,11,30]

Our study findings have to be qualified by the fact that although the sample sizes were rather large, the study populations were not truly selected at random and thus may not accurately represent the at-risk populations. Subjects may have self-selected themselves, which may have resulted in overestimates of HIV prevalence. In addition, obtaining accurate and reliable correlation of risk factors across countries in similar at-risk populations is difficult, because risk practices and willingness to participate may vary from site to site. We attempted to control for this variability by using similar enrollment techniques as well as standardized questionnaires that were at least 90% congruent between countries.

All study subjects were asymptomatic at the time of enrollment. Thus, we strongly believe that we have estimated HIV prevalences and associated risks in a reliable manner. We have not been able to obtain data from Brazil, the country in South America with the highest number of reported HIV infections,[2,4] because of funding and accessibility issues.

We found that the prevalence of HIV infection among FCSWs was extremely low throughout the region (ranging from 0% in several sites to 6.3% in Buenos Aires). A possible explanation for this low prevalence may be the vigorous efforts on the part of MOH-directed AIDS control programs such as the one in Peru.[31,32] Even though no consistent routine HIV and STD medical screening policies for FCSWs exist across the region, interested NGOs and other groups have organized to provide access to effective preventive measures such as wide-scale implementation of condom distribution and prompt treatment of STIs in this at-risk group.[33,34] In contrast to the low prevalences found among FCSWs, the prevalences among MSM groups were substantially higher (2%–27.8%), reflecting the concentrated nature of the epidemic in most countries of the region. An elevated HIV prevalence was found among MSM in Uruguay (21.8%); however, these participants were principally recruited from the population of street-based practicing male commercial sex workers in Montevideo.

Several risk factors were associated with HIV infection among FCSWs and MSM. Most notable in analyses of FCSWs were the associations with a preceding STI history, number of sexual partners per week, IDU (eg, heroin) and non-IDU (eg, marihuana), alcohol use, and blood transfusions. For MSM, in contrast, the analyses identified a higher number of sexual partners; a preceding STI history; sexual contact with foreigners; and marihuana, cocaine, and alcohol use. Because cocaine is generally not injected, the risk associated with its use was interpreted to be secondary to its enhancing effect on sexual activity.[35] In general, the risk of infection to MSM in South America was largely attributable to the magnifying role of STIs and risky behaviors associated with sexual activity.

We were unable to evaluate the association between HIV seropositivity and condom use given a high number of nonresponses to this type of question when country-specific analyses were performed. After pooled analysis by region was performed (eg, Andean and Southern Cone region analyses separately), however, no significant association between condom use (ie, any use vs. none at all) and HIV infection was found after controlling for age and number of sexual contacts per week.

The risk factor profile varied by geographic region for FCSW subjects but not for MSM subjects. It seems that prior STIs, IDU, alcohol use, and blood transfusions represented important factors in Andean region countries, whereas a multitude of other risk factors, including multiple sexual partners, sexual contact with foreigners, and different types of drug use (IDU and non-IDU), could account for the increased risk in the Southern Cone countries of Argentina, Uruguay, and Paraguay. Thus, patterns of risk seem to vary in different regions for FCSWs, whereas MSM groups seem to represent a more homogeneous population in which sexual exposure and non-IDU use account for the bulk of infections, regardless of geographic region.

Throughout the entire Western Hemisphere, the predominant genetic form in circulation has been subtype B, the subtype common in Western Europe and Australia.[3,11] In Argentina and Uruguay, however, it has recently become apparent that BF recombinants are predominant among infected heterosexuals (female heterosexuals and their male partners), whereas subtype B predominates among MSM.[8–10,15,25] Circulation of different subtypes in different risk groups in the same country has enabled us to be able to examine specific risk behaviors and their association with specific HIV subtypes. Because infection with subtype B is the most common in both risk groups (77% in FCSWs and 92% in MSM), the risk factors for infection as a whole tend to be those for subtype B. The risk of infection associated with a prior STI in both groups is present only for subtype B and not at all for subtype F. This represents a consistent finding that was independently observed in both risk groups and thus may have some biologic significance. A more comprehensive analysis of risk factors associated with subtype B or F infection is in progress using sequenced strains.

The genetics of HIV can reveal the interrelatedness of sexual and drug injecting networks when their members are infected by different subtypes. The results pertaining to IDU are a good example of this. Among FCSWs, where IDU is a major component of the epidemic, the risk is almost entirely for subtype B. Conversely, among MSM, where IDU is not common, the risk is highly significant for subtype F. We can derive from our analyses that the injecting network accessed by FCSWs is infected with subtype B, whereas that for MSM is infected with subtype F. The 2 networks are clearly delineated by subtype and thus seem to have little or no interaction.

The pivotal role that STIs play in enhancing the risk of HIV infection for FCSWs and MSM is striking. A renewed region-wide effort to strengthen STI prevention programs in South America might have a large impact on stemming the continued growth of the HIV epidemic. In many countries, the HIV epidemic began with a smoldering low-level epidemic concentrated only in high-risk groups, which lasted, in some cases, for many years. At some point in the epidemic, the virus made the jump to the general population and entered an exponential growth phase such as has been seen in Thailand and Africa.[11–13] In most of the countries of South America, the epidemic still smolders. A vigorous STI prevention program may be successful in preventing the exponential increase in HIV infection and even lowering the risk of infection to people in high-risk groups.

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APPENDIX

Members of the South American HIV Molecular Surveillance Working Group

NGOs: Claudia Ayala and Henry Ardila†, Liga Colombiana de Lucha Contra el SIDA (LCLCS), Bogota, Colombia; Claudio Gallardo, Fundacion Esperanza, Quito, Ecuador; Orlando Montoya and Efrain Soria, Fundacion Equidad, Quito, Ecuador; Nephtali Arias, Amigos por la Vida, Guayaquil, Ecuador; Ricardo Herrera, Siempre Vida, Guayaquil, Ecuador; Jorge L. Sanchez, Lourdes Kusunoki, Javier Lama, and Rosa Galvan, Asociacion Civil Impacta Salud y Educación, Lima, Peru; Alberto Moscoso, Casa Libertad, La Paz, Bolivia; Eliana Dentone and Rosa Gonzalez, Fundacion Margen, Santiago, Chile; Jose Viñoles, Gerardo Menyu, Gustavo Duran, and Laura Dutour, Fundacion SIDA, Montevideo, Uruguay; and Sergio Maulen and Ruben Marone, Nexo NGO, Buenos Aires, Argentina.

National HIV/AIDS control programs, MOHs: Maria E. Acosta, Quito, Ecuador; Hugo Manrique, Pablo Campos, and Luis Suarez, Lima, Peru; Anabella Arredondo and Edith Ortiz, Santiago, Chile; Nicolas Aguayo, Margarita Villafañe, and Liliana Gimenez, Asuncion, Paraguay; and Margarita Serra, Jose Viñoles, Alejandro Pereira, Virginia Galeano, Sofia Rocha, and Carmen Perez, Montevideo, Uruguay.

Other institutions: Maria E. Pacheco, Belkis Pinto, Carlos Aponte, and Hans Salas, Instituto Nacional de Higiene "Rafael Rangel" (INH-RR), Caracas, Venezuela; Yuraima Villarroel, Ana Michini, and Beau Howell-Muñoz, Corposalud, Isla Margarita, Venezuela; Martha Velandia, Gloria Rey, Jacqueline Acosta, Alfredo Mejia, Franklyn Prieto, and Fernando de la Hoz, Instituto Nacional de Salud, Bogota,

†Deceased.

Colombia; Gloria I. Sanchez, University of Antioquia, Medellin, Colombia; Aracely Alava and Carlos Mosquera, Instituto Nacional de Higiene y Medicina Tropical "Leopoldo Izquieta Perez," Guayaquil, Ecuador; Angel Guevera, Hospital Vozandes, Quito, Ecuador; Eugenio Ramirez and Maritza Rios, Instituto de Salud Pública, Santiago, Chile; Ronald Andrade, Instituto de Laboratorios en Salud (INLASA), La Paz, Bolivia; Alberto Gianella, Ana M. Tambare, and Norma Velasquez, Centro Nacional de Enfermedades Tropicales (CENETROP), Santa Cruz, Bolivia; Adolfo H. Galeano, Instituto de Medicina Tropical (IMT), Asuncion, Paraguay; Jose C. Russi and Dora Ruchansky, Laboratorio Nacional de Referencia, Montevideo, Uruguay; and Maria M. Avila, Mercedes Weissenbacher, Horacio Salomón, and Maria A. Pando, Centro Nacional de Referencia de SIDA (CNRS), University of Buenos Aires, Buenos Aires, Argentina.