

## HUMAN IMMUNODEFICIENCY VIRUS INFECTION IN THE REPUBLIC OF PANAMA

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**Abstract.** Thirty-one documented acquired immune deficiency syndrome (AIDS) cases occurred in Panama during 1984-1987. Twenty-three (74%) patients were homosexual males and all but 2 patients recognized prior to June 1987 have died. To identify risk factors for human immunodeficiency virus infection, 287 male homosexual residents of Panama City were enrolled in a cross-sectional study. Nine had human immunodeficiency virus (HIV) antibody. Travel to the United States, homosexual relations with United States nationals in Panama, and sexual contacts in Panamanian clubs and bars were associated with human immunodeficiency virus infection by logistic regression analysis. Number of different male sex partners per year was identified but did not enter the logistic model at a significant level. To estimate seroprevalence in other high risk populations, 183 Panama City female prostitutes and 55 homosexual males from the rural Azuero peninsula were screened; none were seropositive. Eighty-four percent of Panamanian hemophiliacs had antibody; infection was related to factor VIII transfusions. Two of 182 sickle cell anemia patients and 15 of 7,720 volunteer blood donors were positive.

The epidemiology of acquired immune deficiency syndrome (AIDS) presents 2 general patterns. In the United States, Canada, and European metropolitan centers the disease primarily involves homosexual males, intravenous drug abusers, and transfusion recipients. In Central Africa, heterosexual infection is the most important route of transmission in adults, and there is also frequent vertical transmission.<sup>1,2</sup> Clinical manifestations and the natural history of the disease in Africa may also differ from that in the United States.<sup>1-5</sup> This may be the result of exposure to different environmental pathogens rather than true differences in the course of human immunodeficiency virus (HIV) disease.<sup>6</sup>

AIDS in the tropical Americas has not been well studied. It is important to ascertain whether either of the 2 recognized patterns occurs there. Most countries in the tropical Americas have reported AIDS, with the largest numbers from Haiti and Brazil.<sup>7</sup> Most patients have been gay males from metropolitan areas. However, environmentally the tropical Americas are similar

to Africa, and many areas have predominantly black populations. Early studies implicated Haitians as a high risk group. The impact of sexual promiscuity involving United States gay males and heterosexual/environmental factors among Haitians and other Caribbean populations is not clear.<sup>8-10</sup>

This study reviews all documented AIDS cases in Panama 1984-1987 and reports a cross-sectional seroepidemiologic study identifying risk factors for HIV infection in homosexual males, female prostitutes, multiple transfusion recipients, and volunteer blood donors from Panama City.

### MATERIALS AND METHODS

#### *Study area*

The Republic of Panama is a tropical Caribbean Basin country which geographically and culturally links Central and South America. Panama City is the capital and also the Pacific terminus of the Panama Canal. The capital, with 800,000 residents, contains 33% of the country's population. The Panama Canal Area, which

is part of Panama City, contains mainly United States military personnel and dependents.

### *Study populations*

**AIDS cases.** We identified presumptive AIDS cases diagnosed at hospitals in Panama City in 1982–1987, abstracted clinical data from their hospital charts, and tested sera for HIV antibody. AIDS case definition used CDC standard criteria including HIV serologies, and T4/T8 determinations (when possible). Case ascertainment was excellent because the Ministry of Health and Social Security Administration operate a well organized, horizontally integrated, national health services system throughout the country with an efficient procedure of patient referral from primary level health services to 2 tertiary medical centers (located in the capital).

**Metropolitan gay males.** Between April 1984 and April 1986 we enrolled homosexual males from 4 sources in Panama City: a walk-in clinic which provided free medical consultation (advertised by word-of-mouth in the gay community); a Social Security Sexual Dysfunction Clinic; the city jail; and private physicians (those known to treat gay males were asked to refer all such patients to Gorgas Memorial Laboratory to participate in the survey).

**Rural gay males.** In 1986, we worked with the Department of Family and Community Medicine, School of Medicine, University of Panama to enroll gay males from Herrera and Los Santos provinces in the survey. These provinces comprise the Azuero peninsula, a major sugar cane and cattle industry region.

**Female prostitutes.** We enrolled 183 prostitutes in January–May 1986 as they attended routine weekly Social Hygiene Clinics at the Chorriillo, Río Abajo, Emiliano Ponce, and Boca la Caja District Health Centers.<sup>11</sup> These women have clients from the Canal Area, a commercial seaport, and upper and lower class barrios throughout Panama City. Study subjects were selected according to their order in the Clinic's queue. In 1978–1979 we had conducted a similar study of prostitutes which enrolled 1,233 high risk women; 282 sera from that study were randomly selected to be screened for HIV antibody.

**Multiple transfusion patients.** Two multiple transfusion populations, hemophiliacs and sickle cell anemia patients, were studied. There were 60–70 treated hemophiliacs in Panama; we ob-

tained serum from 19 who are followed at the Hematology Clinic of the Social Metropolitan Medical Center (CHM-CSS).<sup>12</sup> We also included 6 von Willebrand disease patients and 182 sickle cell anemia patients from the clinic.

The Ministry of Health and Social Security Administration screen all blood donated in Panama City for HIV antibody. Data from all donors at the CHM-CSS during January–November 1986 and at Santo Tomás Hospital during November 1985–November 1986 were reviewed; all donors screened as antibody positive were retested.

### *Data collection*

Study protocols were reviewed, approved and monitored by the Gorgas Memorial Laboratory (GML) Human Subjects Committee and by the Ministry of Health. All participants gave voluntary informed consent prior to entering the study.

Each component of the study utilized the same methodology of interview, physical examination, and specimen collection. All data were linked by study numbers only. Each subject was interviewed in his native tongue (Spanish, English, or French) by an experienced technician. Interviews were structured and used a standardized questionnaire.

**Physical examination.** Gay males and female prostitutes received physical examinations from Division of Epidemiology physicians. For the Hematology Clinic patients, data was abstracted from hospital charts; standardized interviews to ascertain risk factors were not conducted.

Vacutainers were used to collect 10–20 ml venous blood; tubes were allowed to clot at room temperature and then held on wet ice for 1–4 hr. Serum was separated at the GML Serum Bank, divided into small volumes, and stored at  $-20^{\circ}\text{C}$  until tested.

Sera were screened at GML using the Electronucleonics ELISA kit for HIV antibody. Putative positives were retested under code after random sorting into another batch; sera twice positive were tested by Western blot at the CDC and only confirmed sera were considered positive. All positive units from the blood banks were rescreened but were not confirmed by Western blot.

Genital, rectal, and oral specimens were obtained from gay males and female prostitutes and

cultured for *N. gonorrhoea*, *C. trachomatis*, mycoplasma, herpes simplex virus (HSV), and cytomegalovirus (CMV). These were processed by the GML Clinical Virology Department using standard laboratory methods.<sup>13</sup>

### Statistical analysis

All data were collected directly on standardized interview and physical exam forms. Personal identifying information was not transcribed. Forms were reviewed, coded, and the data entered into dBASE-III plus (Ashton Tate, Culver City, CA) interactive files. Laboratory results were coded and entered. Statistical manipulations were done using Systat<sup>14</sup> and BMDP-PC (BMD Statistical Software, Inc., Los Angeles, CA).

Chi-square analysis, Fisher's exact test, and odds ratio estimates of relative risks were used to compare the association of individual risk factors with HIV antibody. Stepwise logistic regression analysis was used to determine the combined importance of HIV risk factors identified in univariate analyses.<sup>15, 16</sup>

## RESULTS

### AIDS cases

The first case of AIDS was diagnosed in Panama in July 1984, and 31 confirmed cases were diagnosed through October 1987. The number has doubled each year. Twenty-three patients (74%) were homosexual (21) or bisexual (2) males; 3 gays and 3 heterosexual patients were intravenous drug users; 2 cases were transfusion recipients (1 hemophiliac and 1 woman who had received transfusions in New York); 3 patients, including a Haitian woman, denied known risk factors. The most common opportunistic infections were disseminated histoplasmosis (5), tuberculosis (4), *Pneumocystis carinii* pneumonia (4), disseminated candidiasis (4), CMV pneumonia (2), and toxoplasmosis (1); 6 patients had diarrhea of unspecified etiology and 5 presented with pneumonia and sepsis of unspecified etiology. Seventeen cases died 1–10 months following diagnosis, 2 have been lost to follow-up, and 11 are still alive (9 of which were diagnosed June–October 1987).

### HIV seroepidemiology—prevalence of infection in high risk populations

Nine of the 287 (3.1%) members of the metropolitan gay male study group had HIV antibody detected by the ELISA screening test and all were confirmed by Western blot. None of 54 sera from rural gay males had HIV antibody. None of 183 prostitutes enrolled during 1986 or the 282 enrolled 1978–1979 had antibody.

Sixteen of 19 hemophiliacs (84%) and 1 of 6 von Willebrand patients (17%) had HIV antibody. All patients denied homosexual or bisexual behavior, intravenous drug abuse, and other risk factors other than multiple transfusions. HIV antibody prevalence increased with age.

All hemophiliacs had received multiple transfusions with factor VIII and cryoprecipitate. Factor VIII used at the Complejo Hospitalario Metropolitano (CHM-CSS) for the last several years has been purchased from pharmaceutical companies in the United States. Patients with von Willebrand disease were treated with fresh plasma and locally obtained cryoprecipitate.

Only 2 of 182 sickle cell anemia patients were seropositive for anti-HIV. Both denied homosexual or bisexual activity or intravenous drug abuse. Both patients had received multiple transfusions of locally derived packed red cells.

Fifteen of 7,720 units of blood tested at the CHM-CSS January–November 1986 and 17 of 16,000 units donated at Santo Tomás November 1985–November 1986 had HIV antibody detected by ELISA screen.

### HIV seroepidemiology—gay male risk factors for HIV infection

Within the metropolitan gay male sample, antibody prevalence varied according to various risk factors. Six of 85 (7.1%) walk-in patients had antibody compared to 3 of 201 men recruited from other groups (Fisher's exact test  $P = 0.02$ ). Other factors also varied by enrollment category such as ethnic group, socioeconomic status, and sexual habits; therefore, enrollment category was included in subsequent risk factor analysis.

Various markers of homosexual relationships with males from the United States were highly associated with HIV infection (Table 1). Seroprevalence was greater in subjects who had trav-

TABLE 1  
*HIV antibody rates in Panama City gay males according to contact with U.S. males*

	No. pos./No. tested* (% pos)	
	Entire gay male population	Volunteer clinic group
	Travel to U.S.	
Yes	6/46 (13.0%)	4/12 (33.3%)
No	3/325 (1.3%)	2/71 (2.8%)
Odds ratio	16.1	17.25
95% CI	3.40-54.17	2.17-100.19
	Homosexual relations while in U.S.†	
Yes U.S.	6/15 (40.0%)	4/6 (66.7%)
Yes non-U.S.	0/7	0/2
No	0/22	0/4
	Fisher's exact test $P = 0.01$	Fisher's exact test $P = 0.07$
	Homosexual relations with U.S. in Panama	
Yes	7/96 (7.3%)	5/44 (11.4%)
No	2/189 (1.1%)	1/41 (2.4%)
Odds ratio	7.35	Fisher's exact test $P = 0.12$
95% CI	1.36-35.46	
	Type of U.S. homosexual in Panama‡	
Military	5/46 (10.9%)	4/25 (16.0%)
Others‡	0/32	
Mixed‡	1/14 (7.1%)	

\* Numbers tested may vary due to unknown responses.

† Participants who traveled to the U.S. were asked if they had homosexual relations while in the U.S. and if so, if they had sex with U.S. nationals or only with non-American partners.

‡ Patients were queried as to what type of U.S. nationals they customarily had sex with in Panama: military refers to members of the uniformed services; others refers to Canal Area business men or tourists; mixed includes 14 subjects who did not limit their sexual activity to 1 type of U.S. national, including the 1 seropositive subject in this group who had sex with military as well as others.

eled to the United States (13% positive vs. 1.3% positive in non-United States travelers). HIV antibody prevalence was 40% (6/15) among those who had visited the United States and had engaged in homosexual relations with males; there were no seropositives among the 29 who denied such relations. In addition, HIV prevalence was significantly greater in subjects who had engaged in sexual relations with United States males in Panama than in those who had not (Odds Ratio = 7.35). Travel to the Caribbean, Central and South America, or Africa was not associated with an increased risk of infection with HIV, nor was antibody more common in participants who had sexual relations with nationals from these areas.

Sexual promiscuity was also associated with HIV infection (Table 2). We asked participants to estimate the number of different homosexual partners they had had during the present year and each of the previous 3 years. There was a significant association between number of different partners and infection. We also asked subjects if they "picked-up" sexual partners in gay clubs or bars (never, occasionally, or regularly);

seroprevalence varied according to the intensity of this activity.

HIV antibody prevalence was similar in subjects who were customarily paid for homosexual acts (5/138, or 3.6%) and those who were not (4/148, or 2.7%), and was also similar in men who

TABLE 2  
*HIV antibody prevalence by measures of sexual promiscuity, Panama City gay males\**

Number of homosexual partners in the last year			
No. pos./No. tested (% pos)			
None	One	2-10	>10
0/22	0/42	3/147 (2.0%)	6/72 (8.3%)
Chi-square = 5.1 $df = 3$ $P = 0.03$			
Chi-square for trend = 7.9 $P = 0.005$			
Pick-up sexual partners in gay clubs or bars			
No. pos./No. tested (% pos)			
Never	Occasionally	Regularly	
4/232 (1.7%)	3/37 (8.1%)	2/14 (14.3%)	
Chi-square = 10.1 $df = 2$ $P = 0.006$			
Chi-square for trend = 10.1 $P = 0.001$			

\* Denominators may vary due to unknown responses.

TABLE 3

Relative risk estimates from logistic regression analysis of risk factors for HIV antibody in Panama City gay males

	Odds ratio	95% CI
	Entire study population	
Travel to U.S.	10.18	2.38-43.55
Sex with U.S. males in Panama	6.27	1.23-31.91
	Volunteers only	
Pick-up sex partners in Panamanian gay clubs	33.12	2.93-374.7
Travel to U.S.	20.02	1.79-223.9

paid for homosexual relations (1/39, or 2.6%) vs. those who did not (8/246 or 3.3%).

Specific homosexual practices were not related to HIV infection. These practices include receptive vs. insertive oro-genital sex, receptive vs. insertive anal intercourse, receptive vs. insertive oro-anal intercourse, and fisting.

None of the other sexual behavior risk factors, including age of first homosexual intercourse, marital status (to women), number of female sexual partners per year (current year and previous 3 years), was associated with HIV infection. The majority of the population was exclusively homosexual and none of the antibody positive subjects were bisexual.

We interviewed concerning self perception of health, knowledge of AIDS, and recreational intravenous drug use (which is uncommon in Panama); none of these were associated with infection. We also obtained detailed medical histories including previous episodes of gonorrhoea, urethritis, genital or anal herpes, genital ulcers, genital or anal warts, parasitic infections, diarrhoea, weight loss, adenopathy, cough, and previous hospitalizations or transfusions, and found no association with HIV infection.

The results of the physical examinations were unremarkable. None of the subjects had evidence of AIDS related complex or other significant abnormalities which could be related to infection with HIV.

A stepwise logistic regression model was used to estimate the effects of variables found to be individually associated with HIV antibody. The 4 variables were travel to the United States (yes/no), sexual relations with United States nationals in Panama (yes/no), sexual relations with men picked-up in Panama City gay clubs or bars (yes/never/no-never), and number of different male sex partners in the year prior to study (none, 1, 2-10, >10).

Two hundred seventy-eight of the 284 (98%) participants had complete data and were included. Travel to the United States and sexual relations with United States nationals in Panama were the only variables significantly associated with HIV antibody (Table 3). Since antibody prevalence was higher in men enrolled through the Volunteer Walk-in Clinic, we recalculated the model limited to this group. For 81 of 85 (95%) volunteers with complete data, "picking-up" homosexual partners in Panama City gay clubs or bars and travel to the United States were highly associated with HIV.

With the exception of CMV, no STD agent was associated with anti-HIV. Two of 3 individuals secreting CMV had HIV antibody compared to 6 of 216 CMV-negative participants. Isolation rates for other STDs were low so that it was difficult to make meaningful comparisons with respect to other risk factors. However, no individual agent appeared to be associated with HIV, nor was there a relation between infection with any STD (combining all culture results) and HIV. Overall, 8% (22/279) of the metropolitan males had *Neisseria gonorrhoea* isolated from the rectum, throat, or urethra; *Chlamydia trachomatis* was isolated from 1% (4/268); mycoplasma from 22% (62/282); herpes simplex virus from 5% (13/250), and cytomegalovirus from 1% (3/219). In addition, 16% (45/282) had positive syphilis slide flocculation tests (RPR-Brewer Diagnostics).

The rural gay males were all negative for HIV infection, but showed similarities to those from Panama City with respect to sexual promiscuity and behaviors (number of partners per year, sexual contacts made in clubs and bars, paid for or paying for sex, type of sexual relations). The major difference between this group and the metropolitan males was the degree of sexual contact with outside populations: only one had traveled to the United States in the last year and he denied

having sexual relations while there. Thirty-one (53%) rarely or never visited Panama City. Of those who did travel to Panama City, 18% admitted to having homosexual relations during these visits; 9 (17%) said they had never had homosexual relations with United States nationals in Panama.

#### DISCUSSION

This study has two major conclusions. First, as in other parts of the world, the incidence of AIDS has rapidly increased since the first case was diagnosed in 1984 (a Haitian woman who had immigrated in 1980). The number of cases has doubled annually and involves the same risk groups as in the United States. Clinical presentation has been comparable except that opportunistic infections involve locally endemic organisms.<sup>1</sup> Neurologic manifestations<sup>17</sup> have not been prominent. Second, infection with HIV is largely limited to the same risk groups. The most significant risk factors involve promiscuous homosexual activity with United States nationals, or having hemophilia and receiving multiple transfusions with factor VIII. Heterosexual transmission of HIV is not important in Panama; we have not detected HIV infection in female prostitutes and transmission via local blood products is uncommon.

Approximately 3% of the Panama City gay male population has been infected with HIV. Although overall prevalence was low, stepwise logistic regression analysis showed that having homosexual relations with United States nationals was the most important determinant of infection. Promiscuity, as reflected in making sexual contacts in clubs and bars or having a number of different male sexual partners per year, was important. Similar findings have been reported from other areas.<sup>18</sup> Other risk factors, such as passive anal intercourse, did not appear to be important.<sup>19,20</sup>

Interpretation of these findings, especially negative associations, is restricted by the small sample sizes and low frequencies of seropositivity. Thus, the power to test interaction and confounding between multiple variables was limited. It is possible that other factors are important determinants of infection and disease.

Several weaknesses inherent in the study design should be noted. The most important is unknown sample bias. We sampled the gay male population by recruiting through self-referral

sources. We have not been able to determine the Panama homosexual population and cannot quantify sampling methods. Most subjects were anal recipient sexual partners who rarely practiced insertive intercourse, so an obvious segment of the population was missed.

Another major limitation concerns timing. The AIDS epidemic is just beginning in Panama. At this early stage we would expect risk factors for infection to reflect contact with infected individuals from outside sources. As infection becomes more prevalent, the importance of outside contact may diminish and relative risks associated with locally important sexual practices may appear.<sup>21,22</sup> Gay males in Panama are more conservative sexually than similar populations in United States cities where AIDS incidence is high.<sup>23-25</sup> It will be important to determine how local behavioral and other factors will affect progress of the disease.<sup>26</sup>

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