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The Emerging Role of HTLV-I/II and HIV-1 Among Intravenous Drug Users in Detroit

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During 1987-1988, a seroprevalence study of the human immunodeficiency virus (HIV-1) and the human T-cell lymphoma/leukemia virus (HTLV-I/II) was performed among Detroit intravenous drug users unaffiliated with substance abuse programs. Seroprevalence data along with patient demographic information were compared to a similar study performed in 1985-1986. In the earlier study, 12 (12.5%) of 96 individuals tested positive for HIV-1. Of the 74 available negative samples retested in 1987-1988 for retroviruses, 7 (9.5%) tested positive for HTLV-I/II. Thus, the overall retroviral (HIV-1, HTLV-I/II) seropositive rate for 1985-1986 was 22%. In 1987-1988, 11 (15.7%) of 70 individuals tested positive for HIV-1 and 7 (10%) tested positive for HTLV-I/II. Concomitant infection with both viruses was found in 2 (2.9%) of the 70 individuals. Thus, retrovirus seroprevalence in 1987-1988 was 22.9%. In 1987-1988, significant differences between the retroviral-positive group and the retroviral-negative group consisted of intravenous drug use greater than 16 years ($P = 0.059$) for an odds ratio of 3.80 (CI 1.12-12.89) and sex with female prostitutes ($P = 0.029$) for an odds ratio of 5.38 (CI 1.38-20.95). (Henry Ford Hosp Med J 1992;40:131-5)

One in four individuals with the acquired immunodeficiency syndrome (AIDS) in the United States has used illicit drugs (1). There are an estimated 1.1 million active intravenous drug users (IVDUs) in the United States, but only about 15% receive substance abuse counseling (2). A total of 90% are heterosexual and 30% are women. Of the women, 90% are of child-bearing age and 30% to 50% have engaged in sexual prostitution (3). They represent the major source of perinatal transmission of the human immunodeficiency virus (HIV-1) in the United States (3-7). Seroprevalence of HIV-1 among IVDUs ranges from less than 5% in most geographic areas of the United States to 60% in New York City and surrounding areas (2).

The human T-cell lymphoma-leukemia virus (HTLV-I) is the first human retrovirus to be described. Among the general United States population, less than 1% are infected with HTLV-I (8,9) which shares the same routes of transmission as HIV-1 (10-12). In IVDU populations, however, significantly higher HTLV-I seroprevalence has been demonstrated. Serum specimens collected in 1971-1972 from 1,129 IVDUs from 43 states disclosed a seroprevalence of 6.3% (13). More recently, HTLV-I seroprevalence among IVDUs of New York City ranged from 9% to 23% (14,15). Since HTLV-I cannot be readily distinguished from HTLV-II, we will refer to these two agents collectively herein as HTLV-I/II.

In the metropolitan Detroit area, the Detroit Police Department estimates that there are 30,000 to 40,000 active IVDUs (16). Despite this large IVDU population, relatively few seroprevalence studies for HIV-1 have been conducted, and no sero-

prevalence studies for HTLV-I/II exist. According to available studies, HIV-1 seroprevalence ranged from 4.6% to 12.5% in 1985-1986 and from 7.8% to 13.8% in 1986-1987 (2,16).

This study was undertaken to examine the seroprevalence of both HIV-1 and HTLV-I/II retroviruses in the IVDU population of Detroit, to collect demographic and risk factor information for this population for 1987-1988, and to compare this information with a similar study performed in 1985-1986 (16).

Methods

Patient selection

This study attempted to enroll all patients with an identifiable intravenous drug use history who sought medical assistance in either Henry Ford Hospital's Department of Emergency Medicine or Infectious Diseases Clinic between October 14, 1987, and March 28, 1988. Henry Ford Hospital is a 923-bed acute care facility located in the inner city of Detroit. The hospital maintains an active Emergency Department that services the local area for general medical, trauma, and surgical problems. Patients were included in the study if they admitted to parenteral

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drug abuse within the preceding five years and provided informed consent before having their serum tested for HIV-1 and HTLV-I/II. Informed consent was provided by all patients. Each was interviewed by a physician and completed an anonymous questionnaire detailing individual demographics and drug, sexual, social, and medical histories. Patients were excluded if they had previously tested positive for HIV-1 or been diagnosed with AIDS (Centers for Disease Control criteria).

Serologic screening

Collected serum was stored at -70°C along with serum collected in a similar epidemiologic study performed during 1985-1986. Serologic testing was performed in batches by the same laboratory technicians to minimize laboratory variability in testing. Serum samples were tested for antibodies to HTLV-I/II and HIV-1 by enzyme immunoassay (EIA) using purified viral lysate (Abbott Laboratories, North Chicago, IL). Repeatedly reactive samples by EIA were confirmed by Western Blot. Those EIA-positive samples that were indeterminate or negative by Western Blot methodology were further tested by radioimmunoprecipitation assay (RIPA) using 35_s methionine and cysteine labeled cell lysate (Abbott). Reactive samples by RIPA were also considered positive.

Statistical analysis

Variables from the questionnaire were compared for seropositive and seronegative groups using Fisher's Exact test. Risk ratios and 95% confidence intervals (CIs) were also calculated.

Results

A total of 79 IVDUs were identified and enrolled. Complete data (serum and completed questionnaire) were available for 70 individuals. Patients were excluded if their questionnaires were incomplete or, most commonly, if they voluntarily withdrew from the study after attempted phlebotomy.

A total of 74 (76%) of 96 samples collected in 1985-1986 were available for serologic study in 1987-1988. Of the original 96 specimens, 22 had been consumed while performing HIV-1 serology. The 12 HIV-1 positive specimens collected during that study were among these 22 samples. None of the 74 remaining specimens retested positive for HIV-1 in 1987-1988 (Table 1).

In 1985-1986, therefore, 12 (12.5%) of 96 individuals tested positive for HIV-1. Of the 74 available samples retested in 1987-1988 for retroviruses, 7 (9.5%) of 74 tested positive for HTLV-I/II. The minimum overall retroviral (HIV-1 + HTLV-I/II) seropositive rate for 1985-1986 is estimated to be 22% (Table 1).

In 1987-1988, 11 (15.7%) of 70 individuals tested positive for HIV-1 and 7 (10%) of 70 samples tested positive for HTLV-I/II. Concomitant infection with both viruses was reported in 2 (2.9%) of 70. The overall retrovirus seroprevalence in 1987-1988 was 22.9%. In 1987-1988, significant differences between the retroviral-positive group and the retroviral-negative group consisted of intravenous drug use greater than 16 years ($P = 0.059$) with an odds ratio of 3.80 (CI 1.2-2.89) and sex with fe-

male prostitutes ($P = 0.029$) for an odds ratio of 5.38 (CI 1.38-20.95) (Table 2).

In 1987-1988, the average age was 40.6 years for the retrovirus-positive group and 35.6 years for the retrovirus-negative group. The HIV-1 seropositive group consisted of 11 subjects, nine men and two women. The HTLV-I/II group numbered seven, all men. Black men predominated in this study, reflecting the population served by the hospital's Emergency Department. In 1987-1988, 51.5% of both retroviral-positive and retroviral-negative groups admitted past sharing of intravenous drug paraphernalia (9 [60%] of 15 and 26 [49%] of 53, respectively). Sexual contact with other intravenous drug users did not differ between the retroviral-positive and the retroviral-negative groups (56.3% versus 54.7%, $P > 0.05$). Additionally, six of the retroviral-positive group and 12 of the retroviral-negative group had donated blood at some time in the past. Only two of the retroviral-positive group and one in the retroviral-negative group admitted to previous homosexual or bisexual contact. Other variables that were evaluated include previous illnesses, military service, and imprisonment. These variables were not associated with an increased risk of retroviral infection.

In the 1985 survey, 8 (67%) of 12 HIV-1 positive individuals admitted sharing drug paraphernalia, but only 40 (47.6%) of 84 of the retroviral-negative group admitted the same. Prostitute contact occurred in 3 (25%) of 12 HIV-1 positive individuals and 13 (15.5%) of 84 HIV-1 negative individuals. Homosexual/bisexual contacts were reported by one individual in the HIV-1 positive group and by three in the HIV-1 negative group. No personal data were available for the HTLV-I/II positive individuals from the 1985-1986 survey.

Discussion

IVDUs constitute the second largest population at risk for AIDS (1,2,17,18). A total of 25% of patients with AIDS in the United States have a history of intravenous drug use. Most seroprevalence data among U.S. IVDUs have been obtained from individuals seeking treatment at drug abuse treatment facilities (2,18). Since only an estimated 15% of the 1.1 million IVDUs in the U.S. are involved with treatment, existing HIV-1 seroprevalence data may not be representative of IVDUs as a whole (18-20). Both of our 1985-1986 and 1987-1988 studies were conducted with active IVDUs not currently involved in a detoxification or substance abuse clinic. These data therefore may represent a group more likely to return to intravenous drug use upon discharge from the hospital or emergency room and, for those carrying the retrovirus, to potentially disseminate it.

Detroit's IVDU population is on the upward slope of the epidemic curve of HIV-1 infection and AIDS, as has happened in other metropolitan areas (21). In New York City, HIV-1 seroprevalence of IVDUs increased from 12% in 1978 to greater than 50% by 1984 (20,22). The seroprevalence among the IVDUs of Detroit, which increased from 12.5% in 1985-1986 to 15.7% in 1987-1988, suggests that Detroit may be experiencing a similar increase of which it is not aware because of the lack of accurate, current estimates. It is possible that an anticipated increase in HIV-1 infection could be blunted if IVDUs were in-

Table 1
Seroprevalence of HTLV-I/II and HIV-1 in Detroit

Year	HIV-1	HTLV-I	HTLV-I and HIV-1	Positive HIV-1 or HTLV-I
1985-1986	12 of 96 (12.5%)	7 of 74 (9.5%)	—*	— (22.9%)
1987-1988	11 of 70 (15.7%)	7 of 70 (10.0%)	2 of 70 (2.9%)	16 of 70 (22.9%)

*Twenty-two serum specimens from 1985-1986 were not available for HTLV-I testing.

creasingly aware of the AIDS epidemic from educational programs, word of mouth, or the mass media (3,20,22-24). Awareness could lead to a reduction in exposure to retroviruses through proper cleansing or nonre-use of drug paraphernalia, safe sex practices, or drug use modification (19,24-26).

Our study suggests a prevalence of HTLV-I/II in Detroit's hospitalized IVDU population. Seroprevalence was 9.5% in 1985-1986 and 10% in 1987-1988. HTLV-I has been shown to be endemic in southwestern Japan and further studies demonstrated increased seroprevalence of the virus in Africa, the Caribbean, South America, and the southeastern United States (27-29). Among IVDUs in the United States, prevalence of HTLV-I ranges from 6.3% (13) to 23% (15), compared to a prevalence of 0.028% in the general population (9). In our study, coinfection with both HIV-1 and HTLV-I/II was found in 2.9% of IVDUs.

The clinical implications of simultaneous HTLV-I/II and HIV-1 infection are unclear. Adult T-cell leukemia has been reported in a homosexual male from Trinidad (30), and a T8 lym-

phoproliferative disorder has been reported (31). More recently, polymyositis (32) has been found in a patient infected with both viruses. Further, it has been reported that human peripheral blood lymphocytes infected with HIV-1 in vitro can be induced to produce large quantities of HIV-1 after mitogenic stimulation by HTLV-I virions (33). In theory, dually infected individuals may produce greater quantities of HIV-1 that may result in more severe (HIV-1-related) immunosuppression and enhanced facility to transmit the viruses or accelerate malignant transformation. Correspondingly, with the knowledge that both viruses are transmitted in a similar fashion, it is noteworthy that HIV-1 infections were found in eight of 10 children in households of dually infected parents and in the two spouses of dually infected men (34). However, no evidence of HTLV-I infection was found among these individuals. The difference did not seem to be related to lower numbers of HTLV-I-infected lymphocytes, as all HTLV-I positive adults had a high proportion of HTLV-I-infected cells when compared to other HTLV-I-infected indi-

Table 2
Demographic Information Among Intravenous Drug Users of Detroit: 1987-1988

	HIV-1	HTLV-1	HIV-1 or HTLV-1	Negative	Odds Ratio	95% Confidence Interval
N = 70	11	7	16	54		
Age (years) (mean ± SD)	39.7 ± 5	42.5 ± 5	40.6 ± 5	35.6 ± 7		
Male:Female	9:2	7:0	14:2	36:18	3.50	0.72-17.09
Black:White	9:2	7:0	14:2	41:12	2.05	0.41-10.30
Length IVDU (years) (mean ± SD)	13.3 ± 7	15.1 ± 7	13.3 ± 7	10.6 ± 6		
IVDU > 16 years	5/11	4/7	7/16	9/53	3.80	1.12-12.89*
Shared paraphernalia	6/11	4/6	9/15	26/53	1.56	0.49-4.99
Past Illness:						
Endocarditis	2/11	4/7	5/16	9/53	2.22	0.62-7.97
Abscess	6/11	3/7	8/16	17/53	2.12	0.68-6.60
Pneumonia	3/11	3/7	5/16	8/53	2.56	0.70-9.36
Hepatitis B seropositive	1/8	0/5	1/12	4/48	1.00	0.10-9.86
Sexual Behavior:						
Sex with bisexual	0/9	2/5	2/14	1/46	2.50	0.20-31.00
Sex with IVDU	6/11	4/7	9/16	29/53	1.06	0.35-3.28
Sex with female prostitute	3/9	3/6	6/14	6/49	5.38	1.38-20.95†
Other:						
Military	4/10	3/6	6/14	8/51	4.03	1.10-14.79‡
Prison	3/10	3/7	5/15	12/46	1/42	0.40-4.99
Donated blood	2/10	4/6	6/15	12/51	2.17	0.64-7.33
Received blood	4/11	4/7	7/16	17/46	1.33	0.42-4.21

*P = 0.059.

†P = 0.029.

‡P = 0.068.

viduals (34). When additional dually infected individuals are identified and clinical cases develop, further studies should clarify the implications of coinfection with HTLV-I and HIV-1.

The sharing of drug paraphernalia by IVDUs has been implicated in the spread of retroviruses (3,12,18,24,35). Approximately 50% of both the retroviral-positive and retroviral-negative groups in the present study admitted to sharing drug paraphernalia. By contrast, in 1985-1986, 75% of Detroit's HIV-1 positive IVDUs reported sharing paraphernalia, while only approximately 50% of the HIV-1 negative group admitted to this practice. Clearly, the high rate of needle/syringe sharing among all groups in both studies represents continued significant risk for retroviral transmission among IVDUs. In addition, about half of both retroviral-positive and retroviral-negative individuals report sex with other IVDUs. While sexual activity represents another avenue for potential retroviral spread among the IVDU population, non-IVDU sexual partners among Detroit's IVDUs are clearly also at risk.

A significantly greater percentage of retroviral-positive individuals in 1987-1988 had contact with female prostitutes (48% versus 12%, $P = 0.0288$), while prostitute contact was not associated with retroviral infection in 1985-1986. Although reasons for this difference are unknown, the implications are that prostitutes can become an important reservoir for transmission not only for their sexual partners but for their children as well.

Certain limitations exist in comparing the present study with that of 1985-1986. Since the latter survey involved hospitalized individuals, there may exist a selection bias for "sicker" IVDUs who may represent a population more likely to be seropositive. Therefore, it is possible that the apparent small increase in the HIV-1 prevalence reported in the current study underestimates the true change that would occur if the groups were strictly comparable. Demographic information is not available for any of the HTLV-I/II positive individuals in 1985-1986 nor is HTLV-I/II seroprevalence available from the 22 HIV-1 positive individuals for that study. This information would be valuable in profiling more completely the retroviral-positive (HIV-1, HTLV-I/II) groups of 1985-1986.

Another selection bias introduced in the study was the exclusion of known HIV-positive or AIDS cases. This was consistent with the effort to establish the prevalence of unknown HIV cases. Because a community survey of IVDUs cannot be done without significant danger to the researchers, the bias of studying only hospitalized patients was accepted in order to estimate the prevalence of retroviral infection among IVDUs.

Containing and controlling communicable diseases is a desirable public health goal. Studies of retrovirus among high-risk groups in non-epidemic settings are necessary to plan for future health care needs as well as to determine the resources required for educational programs that may help halt further transmission.

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