

# Articles

## Seroepidemiology of Viral Infections Among Intravenous Drug Users in Northern California

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Intravenous drug users are frequently exposed to parenterally transmitted viral infections, and these infections can spread to the general population through sexual activity. We investigated the prevalence of serologic markers for human immunodeficiency virus type 1 (HIV-1), human T-cell lymphotropic virus type I/II (HTLV-I/II), hepatitis B virus (HBV), and hepatitis C virus (HCV) in intravenous drug users and their sexual contacts. Of 585 drug users from northern California tested for these serologic markers, 72% were reactive for the antibody to HCV, 71% for the antibody to hepatitis B core antigen, 12% for HTLV-I/II antibodies, and 1% for the HIV-1 antibody. The prevalence of serologic markers for these four viruses correlated with the duration of intravenous drug use, the ethnic group, and the drug of choice. More than 85% of subjects infected with either HCV or HBV were coinfecting with the other virus. All persons reactive to HTLV-I/II antibodies had antibodies for either HBV or HCV. Of 81 sexual contacts tested, 17% had evidence of HBV infection while only 6% were reactive for HTLV-I/II antibodies and 4% for the antibody to HCV. None of this group was infected with HIV-1.

We conclude that HTLV-I/II and HCV are inefficiently transmitted to sexual contacts while HBV is spread more readily. Programs designed to discourage the sharing of drug paraphernalia, such as needle and syringe exchanges, should decrease the risk of parenterally spread viral infections in intravenous drug users and thus slow the spread of these infections to the general population.

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**I**ntravenous (IV) drug users acquire parenterally transmitted viral agents often by sharing needles, syringes, and other paraphernalia.<sup>1</sup> Regional differences in the prevalence of human immunodeficiency virus type 1 (HIV-1) infection in IV drug users reflect the date of introduction of the infection and the manner in which drug paraphernalia are shared.<sup>2-10</sup> In the United States, regional variation of the prevalence of antibody to human T-cell lymphotropic virus type I and II (HTLV-I/II) has been observed.<sup>11-13</sup> Horizontal, vertical, and blood-borne vectors of the transmission of HTLV-I/II have been reported.<sup>10-17</sup> Both hepatitis B and C viruses are transmitted parenterally.<sup>18,19</sup> Thus, IV drug users are at risk for acquiring all four infections.

We have studied the demographics and sharing patterns of IV drug users in the Sacramento, California, area and have determined the prevalence of several parenterally transmitted viral infections in these persons and some of their drug-free sexual contacts who participate in drug treatment programs. These infections are hepatitis B virus (HBV), hepatitis C virus (HCV), HTLV-I/II, and HIV-1. The duration of IV drug use and the relative ease by which these agents are transmitted sexually and parenterally determine the prevalence of these infections in the different drug-injecting groups in northern California.

### Subjects and Methods

#### Subjects

The target population consisted of persons enrolled in the two major drug treatment programs (outpatient methadone

detoxification and maintenance program and residential 21-day detoxification and long-term drug-free program) in Sacramento, from August 1987 to June 1989. These persons were offered education regarding the acquired immunodeficiency syndrome (AIDS) and testing for HIV-1 antibody at no cost. Fliers regarding the study were posted, and all staff members were informed about the study. The University of California, Davis, has an ongoing project to assess the effect of intensive, repeated AIDS prevention education on the spread of HIV-1 among IV drug users and their sexual partners. Persons who identified themselves as either an IV drug user or a sexual partner of one and who volunteered to participate were admitted into the program.<sup>20</sup> No tally was made of those persons who declined, and no attempt was made to discover their reasons for nonparticipation. To be admitted into the treatment programs, these persons acknowledged having self-administered illicit parenteral drugs at least once. Of the IV drug users studied, 97% were habitual users of illicit intravenous drugs. Because the remaining 3% who do not habitually use drugs did not affect our conclusions, we have included them in our analysis.

The study has five components of interactions with drug users: pretest counseling, behavioral data collection, serologic testing, posttest counseling at the time the results are released, and retesting and counseling four or more months after the first visit. During the pretest counseling session, each person was informed about the risk of infection, HIV transmission, methods of preventing transmission, and the HIV antibody blood test. Along with demographic informa-

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## ABBREVIATIONS USED IN TEXT

AIDS = acquired immunodeficiency syndrome  
 anti-HBc = antibody to hepatitis B core antigen  
 anti-HBs = antibody to hepatitis B surface antigen  
 EIA = enzyme immunoassay  
 HBsAg = hepatitis B surface antigen  
 HBV = hepatitis B virus  
 HCV = hepatitis C virus  
 HIV-1 = human immunodeficiency virus type 1  
 HTLV-I/II = human T-cell lymphotropic virus type I and II  
 IV = intravenous

tion, confidential behavioral data were collected on drug use and paraphernalia sharing habits, disinfection techniques, and sexual practices during a one-on-one interview by research staff using a standardized questionnaire.

After informed consent was obtained, blood was drawn for testing from 585 IV drug users and 81 persons who denied personal IV drug use but who were sexual partners of drug injectors either occasionally (11 persons) or for prolonged periods (70 persons). These blood specimens were subsequently tested for serologic markers for HBV, HCV, HTLV-I/II, and HIV-1. Non-drug-using sexual partners who participated in the project came to the program either with their partners or by themselves as they perceived their own risk for HIV infection. All of the participants denied homosexual contacts.

*Serologic Assays*

Serum specimens were obtained from the 585 IV drug users and 81 sexual partners of IV drug users. All serum was frozen immediately after separation from the cellular elements of blood and stored below  $-20^{\circ}\text{C}$  before analysis. These specimens were tested for hepatitis B surface antigen (HBsAg, Auszyme, Abbott Laboratories, Inc, North Chicago, Ill) and for antibodies to the hepatitis B core antigen (anti-HBc, Corzyme, and anti-HBs, Ausab, Abbott Laboratories), hepatitis C (anti-HCV, Ortho HCV ELISA Test System, Ortho Diagnostic Systems, Inc, Raritan, NJ), HIV-1 (anti-HIV-1, enzyme immunoassay [EIA] by Genetic Systems, Seattle, Washington, and Western blot by University of California, Davis, Virus Laboratory done according to Centers for Disease Control criteria), and HTLV-I/II (anti-HTLV-I/II, HTLV-I EIA Diagnostic Kit, Abbott Laboratories, and confirmed by immunofluorescent assay<sup>21</sup> performed by the California Department of Health Services Viral and Rickettsial Diseases Laboratory using in-house reagents).\*

*Statistical Methods*

The combined effects of age, number of years of IV drug use, ethnic group, drug of choice, and sex were studied with multiple logistic regression. Only effects significant at  $P < .05$  are reported. The data were maintained on a Paradox data base and analyzed with the Statistical Analysis System<sup>22</sup> software library and the Biomedical Computer Programs logistic regression program.<sup>23</sup>

**Results***Intravenous Drug Users*

A total of 585 heterosexual IV drug users were evaluated for four parenterally acquired viral infections (Table 1). The

average age of this group was 33 years. Although most (60%) were men, there was no difference in the prevalence of serologic markers by sex. Most drug injectors (74%) were white. Most (74%) had at least a high school education, but 72% were unemployed. Heroin was used by 76%. The members of this group had lived in the Sacramento metropolitan area for an average of 11 years. Nearly all (94%) shared their paraphernalia at least occasionally, usually within their own ethnic group.

The most prevalent serologic markers among IV drug users were anti-HCV (421 of 585 [72%]) and anti-HBc (417 of 585 [71%]; Figure 1). The univariate analyses are shown in Table 2, and the logistic regressions of the same data are shown in Table 3. For the categorical factors, the logistic regression results are displayed as adjusted odds ratios for each category versus a baseline group. For years of IV drug use, the relative odds for each additional five years are given. Also given are the  $z$  statistics (coefficient or standard error) produced by the logistic regression program. The logistic results generally confirm the univariate analyses.

Of the 585 IV drug users, 70 (12%) were reactive to HTLV-I/II antibodies, with a greater prevalence of this marker in African Americans and Hispanics than in whites. The frequency of anti-HBs was significantly higher in Hispanics than in either whites or African Americans. As of June 1989, only 8 (1.4%) of the IV drug users were reactive to the HIV-1 antibody.

The presence of each viral marker except HBsAg corre-

TABLE 1.—Demographic Data on Intravenous (IV) Drug Users in Sacramento, California (n = 585)\*

Demographics	Patients, No. (%)
<b>Sex</b>	
Men .....	344 (59)
Women .....	241 (41)
<b>Ethnic origin</b>	
White .....	430 (74)
Hispanic .....	100 (17)
African American .....	30 (5)
Asian .....	9 (1.5)
Native American .....	7 (1)
Other .....	9 (1.5)
<b>Education, grade</b>	
< 12 .....	152 (26)
12 .....	262 (45)
> 12 .....	171 (29)
<b>Drug history</b>	
<b>IV drug of choice</b>	
Heroin .....	446 (76)
Amphetamines .....	88 (15)
Cocaine .....	41 (7)
Other .....	10 (2)
<b>Sharing of paraphernalia</b>	
Never .....	33 (6)
Sometimes .....	276 (47)
Often .....	68 (12)
Usually .....	79 (14)
Always .....	116 (20)
Not known .....	13 (2)
<b>Disinfection</b>	
Never .....	168 (29)
Sometimes .....	137 (23)
Often .....	29 (5)
Usually .....	89 (15)
Always .....	122 (21)
Not known .....	40 (7)

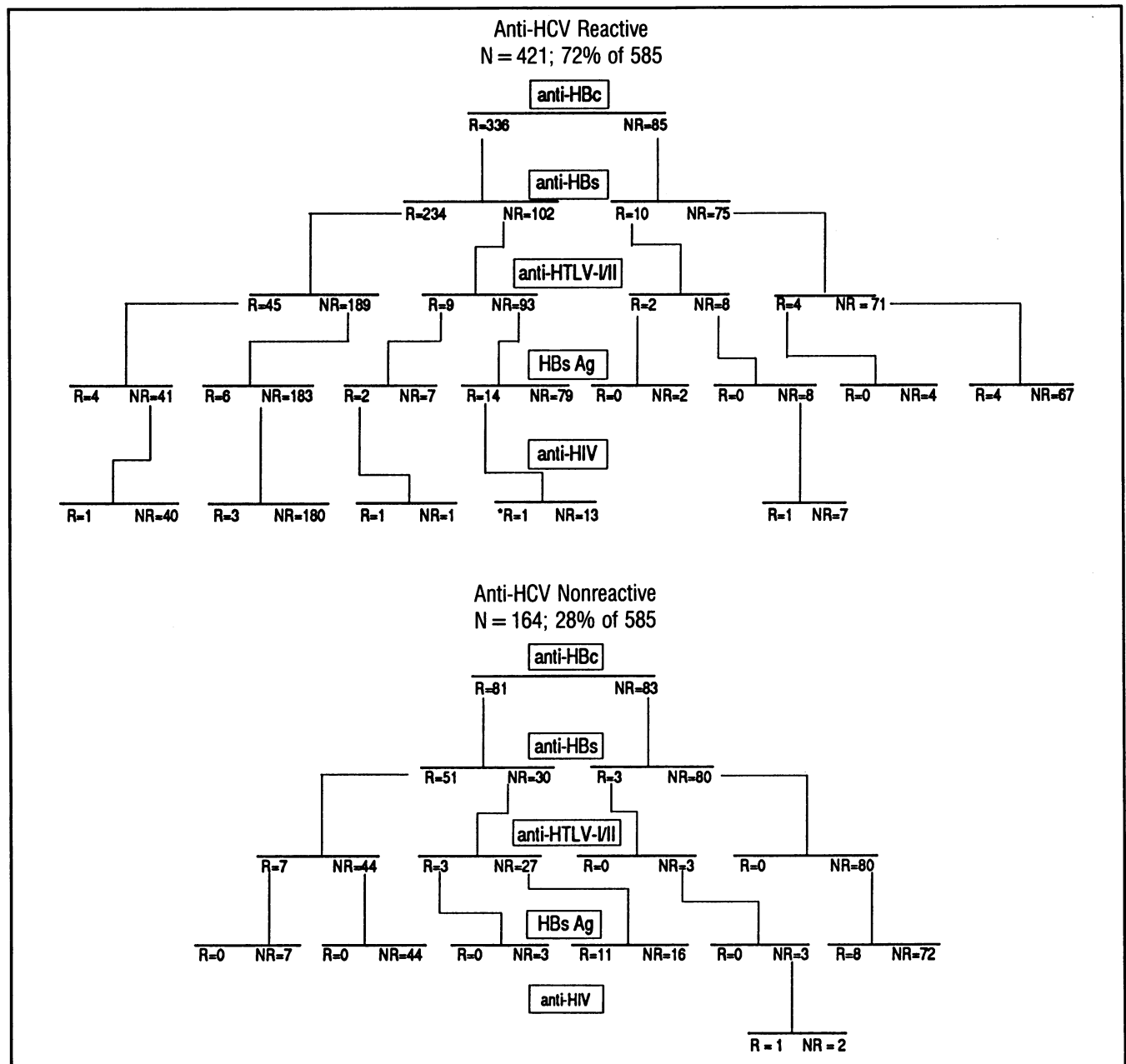
\*Average duration of drug use, 15 years; average duration of IV drug use, 11 years.

\*Abbott Laboratories, Inc, and Ortho Diagnostic Systems, Inc, donated the immunoassays.

lated with the duration of intravenous drug use (Figure 2). This is most apparent in the 188 IV drug users with less than five years of drug use who lack the HIV-1 antibody entirely. They began the parenteral use of illicit substances after publicity about the possibility of contracting AIDS through needle sharing was widespread. The 336 IV drug users who had serologic markers for both HBV and HCV (57% of participants) averaged 13 years of injecting drugs compared with an average of only 4.6 years for the 83 (14%) who lacked markers for both. Every five years the adjusted odds of acquiring a viral infection increased by 100% based on anti-HCV reactivity, by 50% based on anti-HTLV-I/II reactivity, by 80% with anti-HBs reactivity, and by 40% with anti-HBc reactivity (Table 3). The current practice of needle and syringe disinfection did not significantly affect the distribution of

viral markers. This may be due to the recent (within the past three years) introduction of disinfection practices in this population. We are continuing to study this population for evidence of the effectiveness of disinfection in preventing the spread of these diseases.

The years of IV drug use correlated more strongly with the acquisition of serologic markers for HTLV-I/II, HCV, and HBV than did the age of the user. The odds ratios and  $z$  statistics for the risk of each additional five years of age are all lower than the corresponding statistics for years of IV drug use. Age correlates less closely because persons in a particular age group differ in their drug use. For example, people older than 50 years had used drugs for 2 to 52 years, and most people younger than 20 years had used drugs for more than 5 years. Intravenous heroin users had a higher



**Figure 1.**—The schema shows the prevalence of hepatitis B surface antigen (HBsAg) and antibodies to hepatitis C virus (anti-HCV), hepatitis B core [antigen] (anti-HBc), HBsAg (anti-HBs), human immunodeficiency virus (anti-HIV), and human T-lymphotropic virus types I and II (anti-HTLV-I/II) in 585 intravenous drug users, initially stratified by anti-HCV reactivity. NR = nonreactive, R = reactive, \*female

**TABLE 2.—Prevalence of Serologic Markers by Ethnic Group in Intravenous Drug Users**

Ethnic Group	n	HBsAg* No. (%)	Anti-HBc† No. (%)	Anti-HBs‡ No. (%)	Anti-HCV† No. (%)	Anti-HTLV-I/II§ No. (%)	Anti-HIV-15 No. (%)
White	430	35 (8)	301 (70)	212 (49)	298 (69)	35 (8)	5 (1)
Hispanic	100	8 (8)	77 (77)	63 (63)	83 (83)	22 (22)	1 (1)
African American	30	4 (13)	22 (77)	12 (40)	23 (77)	9 (30)	2 (7)
Other¶	25	2 (8)	17 (68)	11 (44)	17 (68)	4 (16)	0 (0)
TOTAL	585	49 (8)	417 (71)	298 (51)	421 (72)	70 (12)	8 (1)
P¶		NS	NS	<.01	<.05	<.0001	NS

Anti-HBc = antibody to hepatitis B core [antigen], Anti-HBs = antibody to hepatitis B surface [antigen], Anti-HCV = antibody to hepatitis C virus, Anti-HIV-1 = antibody to human immunodeficiency virus, Anti-HTLV-I/II = antibody to human T-lymphotropic virus I and II, HBsAg = hepatitis B surface antigen

\*Confirmed positive by neutralization.  
 †Reactive more than once on enzyme immunoassay.  
 ‡Confirmed by indirect fluorescent antibody test except 1 white, or 34 (8%) positive, and 2 Hispanics, or 20 (20%) positive, for a total of 67 (12%).  
 §Confirmed positive by Western blot using Centers for Disease Control criteria for anti-HIV-1.  
 ¶Other includes Asian Americans, Native Americans, and people whose ethnic origin could not be classified.  
 ¶The prevalence of the serologic markers for anti-HTLV-I/II in whites is compared with that in blacks and Hispanics, and the prevalence for anti-HBs and anti-HCV in Hispanics is compared with that in whites. Comparisons in the prevalence of other serologic markers were not statistically significant (NS).

prevalence of both HBV and HCV markers than persons who used IV amphetamines, cocaine, or other substances (Figure 3). This difference is independent of years of IV drug use (Table 3), despite the observation that the duration of drug use for heroin addicts (12.6 years) was greater than that for users of either amphetamines (7.2 years) or cocaine (5.5 years).

Serologic evidence of coinfection with HBV, HCV, and

HTLV-I/II was common (Figure 4). Overall, 336 IV drug users (57%) were reactive to both anti-HBc and anti-HCV; 54 (9%) showed evidence of coinfection with all three viruses (HBV, HCV, and HTLV-I/II). By far the greatest correlation is seen between HBV and HCV, where 81% of the 417 anti-HBc-reactive subjects were also reactive to anti-HCV and 80% of the 421 reactive for anti-HCV were also anti-HBc reactive. In addition, all 70 people reactive to anti-HTLV-I/II were also reactive for either anti-HBc (14%), anti-HCV (9%), or both (77%).

All eight persons positive for the HIV-1 antibody (7 men, 1 woman) were reactive to anti-HCV. Seven of the eight had serologic evidence of current or previous HBV infection, and the eighth (who was reactive only for anti-HBs) probably had been immunized with hepatitis B virus vaccine.

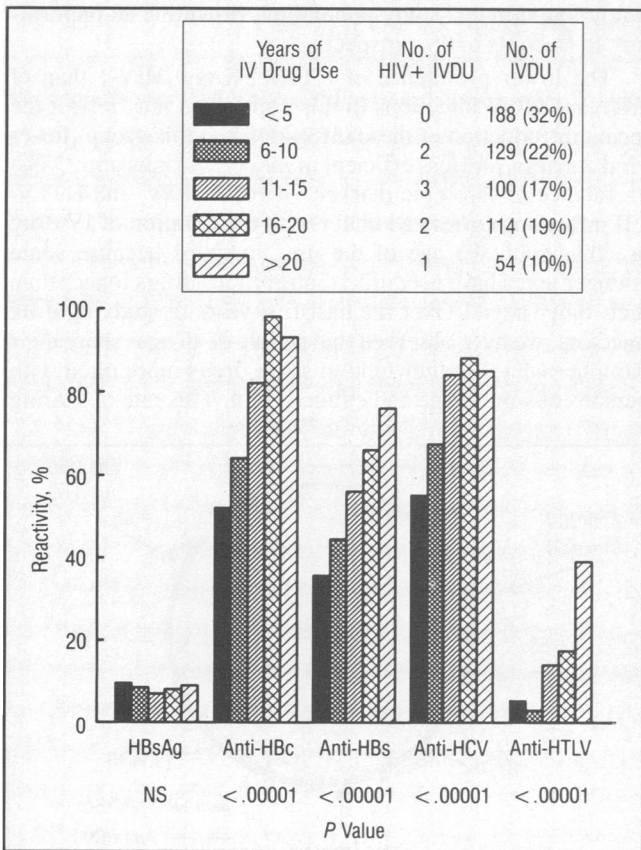
**Sexual Contacts**

Eleven persons (6 men and 5 women) reported rare or infrequent sexual contacts with an IV drug user. Of these, three men and four women (63%) were completely seronegative. One woman was anti-HCV reactive. Three men were reactive for the HTLV-I/II antibody and one of the three was anti-HBc reactive as well.

Of the 70 persons who reported frequent sexual contact with drug injectors, none were HIV-1 infected and 53 (76%) were completely seronegative for viral infection. Three persons (4%) were reactive for anti-HCV, 13 (19%) had serologic evidence of HBV infection, and 4 (6%) were reactive to HTLV-I/II. One was coinfecting with HBV and HCV, and another was reactive to both anti-HBs and anti-HBc (probably a resolved hepatitis B infection).

**Discussion**

The prevalence of viral infection among IV drug users in drug treatment programs during 1988 and 1989 in the Sacramento metropolitan area differed from that in other areas in California<sup>10</sup> and in the United States<sup>7</sup> in the low prevalence (1%) of antibodies to HIV-1 and the relatively low prevalence of antibodies to HTLV-I/II. These retroviruses, as well as both HBV and HCV, are assumed to be transferred readily when IV drug users share paraphernalia. Therefore, the finding that HIV-1 has not yet become well established in this community provides an opportunity to prospectively evaluate



**Figure 2.**—Serologic markers for parenterally transmitted viral infections are correlated with the duration of intravenous (IV) drug use. Anti-HBc=antibody to hepatitis B core [antigen], Anti-HBs=antibody to hepatitis B surface [antigen] (HBsAg), Anti-HCV=antibody to hepatitis C virus, Anti-HTLV=antibody to human T-lymphotropic virus, HIV+=human immunodeficiency virus positivity, IVDU=IV drug user, NS=not significant

TABLE 3.—Odds Ratios for Risk Factors Adjusted for All Other Factors (versus Baseline Group) and z Statistics (Coefficient/Standard Error) From Logistic Regression of Seroprevalence of Virus Markers

Risk Factor	Anti-HTLV I/II		Anti-HCV		Anti-HBc		Anti-HBs	
	Odds Ratio	z	Odds Ratio	z	Odds Ratio	z	Odds Ratio	z
<b>Ethnic group (versus white)</b>								
African American . . . . .	8.2	3.8	3.2	2.1	1.3	0.6	0.5	-1.6
Hispanic . . . . .	3.7	3.8	2.4	2.7	1.8	1.7	1.7	2.1
Other . . . . .	3.1	1.8	1.0	-0.1	0.9	-0.2	0.8	-0.6
Female versus male . . . . .	1.6	1.4	1.2	0.7	0.9	-0.8	0.9	-0.3
<b>Drug of choice (versus amphetamine)</b>								
Cocaine . . . . .	7.5	1.7	1.0	0.5	1.1	0.3	1.3	0.6
Heroin . . . . .	5.6	1.7	2.7	3.8	2.8	3.9	2.2	2.9
Each 5 years of intravenous drug use . . . . .	2.0	6.5	1.5	4.8	1.8	6.5	1.4	4.7

Anti-HBc = antibody to hepatitis B core [antigen], Anti-HBs = antibody to hepatitis B surface [antigen], Anti-HCV = hepatitis C virus, Anti-HTLV-I/II = antibody to human T-lymphotropic virus I and II

interventional programs such as needle exchange and disinfection practices. This low prevalence presents a unique opportunity to prevent further HIV transmission such as has been observed in other similar areas with low prevalence.<sup>24</sup>

Serologic studies of IV drug users in the Sacramento region show a high prevalence of HBV and HCV, with a high probability of dual or multiple infections with these two viruses. Although we used a first-generation enzyme immunoassay for anti-HCV, which has a substantial number of

false-positive and false-negative test results, supplemental testing suggests that more than 85% of anti-HCV EIA-reactive results from IV drug users represent actual infection (Mitchell Nellis, PhD, Ortho Diagnostics, written communication, May 1990). In fact, we may be underestimating the frequency of anti-HCV in this population because first-generation EIA identifies antibodies to only one HCV-related protein. All persons infected with HTLV-I/II had evidence of HBV or HCV infection as well. The antibody to HIV-1 was rarely found in this study population, providing an opportunity to trace its entry prospectively.

The lower prevalence of HTLV-I/II and HIV-1 than of HBV and HCV infections in this population may reflect the recent introduction of these infections into this group, fewer viral carriers, and less efficient modes of transmission.<sup>11</sup> The prevalence of serologic markers of HBV, HCV, and HTLV-I/II infections correlated better with the duration of IV drug use than with the age of the user, perhaps because some younger users have used illicit intravenous drugs longer than their older peers. Over the past five years of studying drug injectors, we have observed that people of all ages share their paraphernalia, but they tend to share drugs more often with persons of similar age and ethnic origin. This rate of sharing

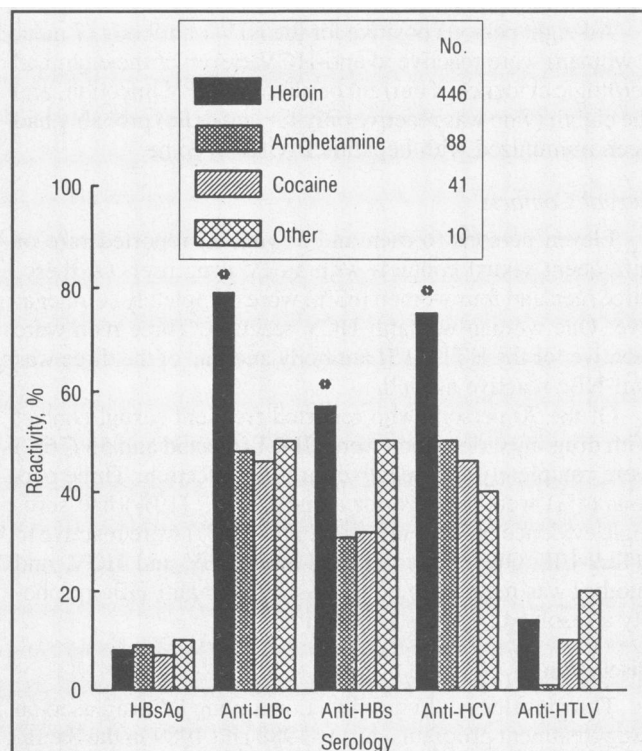


Figure 3.—Serologic markers for parenterally transmitted virus infection are correlated with the type of illicit drug used. "Other" includes intravenous barbiturates, hallucinogens, and marijuana. The asterisk (\*) means that the difference in the prevalence of these markers between heroin and cocaine and amphetamine users is statistically significant ( $P < .00001$ ). The prevalence of other markers between the drugs of choice is not statistically significant ( $P > .05$ ). Anti-HBc = antibody to hepatitis B core [antigen], Anti-HBs = antibody to hepatitis B surface [antigen] (HBsAg), Anti-HCV = antibody to hepatitis C virus, Anti-HTLV = antibody to human T-lymphotropic virus

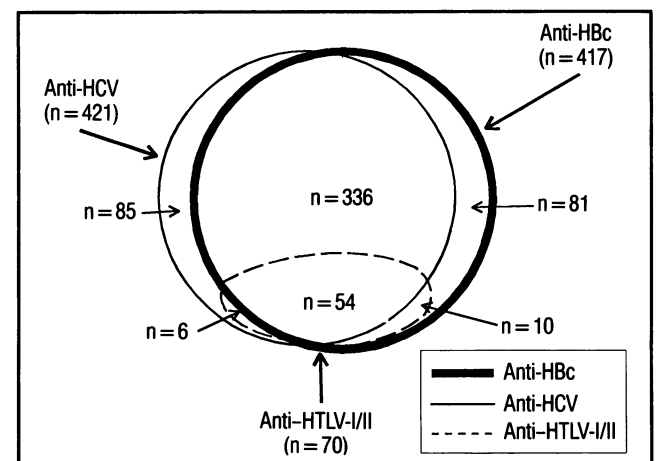


Figure 4.—A Venn diagram shows the prevalence of serologic markers for antibodies to hepatitis B virus core antigen (Anti-HBc), hepatitis C virus C100 peptide (Anti-HCV), and proteins to human T-lymphotropic virus types I and II (Anti-HTLV-I/II).

is much higher than that reported in the IV drug use study from New York City.<sup>2,5</sup> It also may reflect the high prevalence of HTLV-I/II infection in subjects aged 50 years or older regardless of their duration of IV drug use.

The finding that approximately 9% of subjects are HBsAg-positive regardless of the duration of IV drug use, ethnic group, and drug of choice may indicate that a small percentage of these patients have chronic HBV infection or that few are experiencing acute hepatitis B at any one time. The high frequency of HBV and HCV exposure in IV drug users supports the continued use of anti-HBc testing as a surrogate marker for hepatitis non-A, non-B infection in blood donors, even with the introduction of anti-HCV screening using an enzyme immunoassay technique.

The sexual transmission of hepatitis C occurs less frequently than that of hepatitis B, as previously reported.<sup>25,26</sup> Koff and co-workers reported that 23% of sexual partners of IV drug users had evidence of hepatitis B<sup>26</sup>; this is similar to our finding of a 17% HBV infection rate. Only 4% of sexual partners had HCV markers, however, despite a similar prevalence of anti-HBc (71%) and anti-HCV (72%) serologic markers in IV drug users.

As is true for other metropolitan areas, the ethnic composition of IV drug users in the Sacramento metropolitan area is not known. According to a 1990 report ("AIDS in Sacramento County Through 1989," by Mark D. Starr, DVM, MPVM, epidemiologist for Sacramento County Health Department), the population in Sacramento County is 71% white, 8% African American, 11% Hispanic, and 10% other. If IV drug users' ethnicity is similar to that of the general population, then in this study African Americans may be slightly underrepresented and Hispanics slightly overrepresented. Despite these drawbacks, the results from this study of persons in drug treatment programs can be compared with those of studies from other regions of the country that examined similar populations. Because we did not select our patients, other than to solicit participation of all members of drug treatment programs, we can assume that the group studied reflects the population of IV drug users in Sacramento who seek help for their addiction.

The acquisition of viruses by sexual transmission in IV drug users may differ from acquisition by parenteral transmission because of the behaviors that have been described to us by the subjects in our study. They report that although they restrict the sharing of paraphernalia to persons of similar ethnic backgrounds, many drug users interact sexually outside their ethnic and age groups. This may account for the higher prevalence of serologic markers in Hispanics and African Americans than in whites.

In most areas of the country, it is currently illegal for IV drug users to purchase or exchange needles and syringes despite information from the Netherlands and the United Kingdom<sup>27,28</sup> that such practices do not encourage IV drug use, decrease the sharing of paraphernalia, and decrease risk-taking activities during IV drug use. In many states (including California) where possessing needles and syringes without a prescription is a felony offense and is a frequent reason for the arrest of IV drug users, most avoid carrying their own equipment. As a consequence, 94% of these persons share needles and syringes. Our finding of an increased accrual of serologic markers for each parenterally transmit-

ted infection with the duration of IV drug use implies that, if they would stop using drugs intravenously or sharing personal paraphernalia, the spread of many infections should decline.

One of the major goals of the University of California's AIDS Task Force is to decrease the spread of HIV and other parenterally transmitted infections by IV drug use. The prevalence data obtained in this study will serve as a basis for determining whether future interventions prevent or retard the spread of various parenterally transmitted infections.

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