

# HIV-1 Infection in Intravenous Drug Abusers with Clinical Manifestations of Hepatitis in the City of Buenos Aires

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*A serologic study of hepatitis and HIV infections among 99 I.V. drug abusers with hepatitis was conducted between December 1986 and September 1987. The average age of the study subjects was 21 years. Eighty-nine (90%) of the subjects were male, including four whose sexual orientation was homosexual/bisexual. Serologic tests indicated that 87 of the 99 subjects had hepatitis B virus infections, 62 acute and 25 chronic. Nine (10%) of these 87 patients were coinfecting with the delta agent. Two subjects had acute cases of hepatitis A, and the 10 remaining subjects had non-A non-B hepatitis. Forty-seven of the study subjects were also found to be infected with HIV-1. The prevalence of the delta marker was surprisingly high, because Argentina has been regarded as nonendemic for the delta virus. Given the trend of increasing I.V. drug abuse in Argentina, these results presage a significant increase in the delta agent's prevalence in the immediate future.*

**W**orldwide, the group with the highest prevalence of human immunodeficiency virus (HIV) infection, following promiscuous homosexuals, is intravenous (I.V.) drug abusers (1). Part of this group's epidemiologic significance resides in the fact that once HIV infection establishes itself in local I.V. drug abusers, those people can become the primary source for heterosexual transmission of the virus in their area. In addition, I.V. drug abusers are also exposed by the same intravenous route to various other infections—including those caused by hepatitis viruses B, delta, and non-A non-B (2).

Among I.V. drug abusers, notably those in Europe and the United States,

the numbers of AIDS cases occurring and the results of HIV seroprevalence studies point to HIV infection as a growing problem. However, the prevalence of HIV infection among I.V. drug abusers in these two areas varies from place to place—exceeding 50% in some parts of Spain and Italy, for example (2-6), while being lower in other geographic areas of these two countries (7-9) and lower still in other countries, descending to levels such as 6.5% in Scotland (10) and 2.1% in Greece (11).

In Argentina, up to July 1988 a total of 197 AIDS cases had been reported, 12% occurring in people with histories of I.V. drug abuse (12). Overall, the seroprevalence of HIV infection among different groups of Argentine I.V. drug abusers studied has been found somewhat variable but generally high. Specifically, HIV was detected in 22% of a group of I.V. drug abusers enrolled in rehabilitation

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programs in the city of Buenos Aires (13), in 35% of a group of convicts with histories of I.V. drug abuse in a federal prison (14), and in 39% of a group of I.V. drug abusers who spontaneously came forward for HIV consultation in Buenos Aires (15).

Argentine serologic surveys conducted to determine prevalences of infection by HIV and by viruses for B, delta, and non-A non-B hepatitis have approached the problem from different standpoints. At present there are many reports of hepatitis B virus, non-A non-B hepatitis, and asymptomatic HIV infection in groups of drug addicts, and also reports of hepatitis B virus markers in patients infected with HIV. However, few studies have been done of HIV infections among patients with clinical pictures of acute or chronic hepatitis B or non-A non-B hepatitis. Indeed, within Argentina we know of no such published study.

It is also noteworthy that drug abuse has increased substantially in Buenos Aires and its environs, as well as in other urban Argentine communities, in recent years. The result has been an increased incidence of hepatitis types B and non-A non-B within the context of the nation's hepatitis etiology—an increase that has been especially evident among hospitalized patients.

With regard to one particular group of patients, between December 1986 and September 1987 the Hospital de Enfermedades Infecciosas "Francisco J. Muñiz" of Buenos Aires provided medical care to

99 intravenous cocaine abusers with hepatitis. Since intravenous drug addiction alone was known to entail a high risk of HIV transmission, it was decided to study the incidence of HIV infection in this group of I.V. drug abusers who had presented with hepatitis.

## MATERIALS AND METHODS

All of the 99 patients involved presented clinical and humoral pictures consistent with a diagnosis of hepatitis and exhibited transaminase levels 10 times higher than normal. These subjects were selected from among outpatients and inpatients at the Francisco J. Muñiz Hospital during the aforementioned study period.

Information about each subject—including his or her age, sex, sexual orientation, alcohol intake, type and duration of drug addiction, and previous episodes of hepatitis—was entered on a card designed for this purpose.

The determinations provided for each subject included total and differential bilirubin, erythro sedimentation, Quick's test, a complete hemogram, glutamic-oxaloacetic transaminase (GOT), glutamic-pyruvic transaminase (GPT), and alkaline phosphatase (AP). The presence or absence of certain immunologic markers—hepatitis B surface antigen (HBsAg), antibody to hepatitis B core antigen (anti-HBc), anti-HBc IgM, IgM antibody to hepatitis A (anti-HA IgM), and total anti-delta antibody—was deter-

**Table 1.** Sex, average age, and sexual orientation of the 99 intravenous drug abusers with clinical hepatitis constituting the study population.

Sex	No.	Average age (years)	Sexual orientation	
			Heterosexual	Homosexual/bisexual
Male	89	21	85	4
Female	10	20	10	0
Total	99	21	95	4

mined by means of enzyme-linked immunosorbent assay (ELISA) testing that employed the Auszyme, Corzyme, Corzyme-M, anti-delta, and HAVAB-M kits commercially available from Abbott Laboratories. Subjects with hepatitis A IgM antibody (anti-HA IgM+) were classified as having hepatitis A. Those with HBsAg and anti-HBc were classified as having hepatitis B—acute hepatitis B if anti-HBc IgM was present, chronic hepatitis B if it was absent (16). Subjects serologically negative for hepatitis A virus, hepatitis B virus, cytomegalovirus, and Epstein-Barr virus were classified as having non-A non-B hepatitis.

The presence of HIV-1 was determined using three tests for screening and one for confirmation. More specifically, test sera were screened using commercial enzyme immunoassay kits from two manufacturers (Virgo HTLV-III ELISA produced by Electronucleonics Inc., Fairfield, NJ, USA, and Vironostika anti-HTLV-III Microelisa System made by Organon Teknika, Turnhout, Belgium) together with one gelatin particle agglutination kit (Serodia HIV produced by Fuji Rebio Inc., Tokyo, Japan).

Sera yielding negative results with all three screening methods were classified as negative for HIV. Those yielding positive results by one or more methods were confirmed by the Western blot test (Biotech/Dupont HIV). This latter test

**Table 2.** Intravenous drugs used by the 99 study subjects.

Drugs	Study subjects	
	No.	(%)
Cocaine alone	89	(90)
Cocaine + morphine	4	(4)
Cocaine + heroin	1	(1)
Cocaine + 2 or more drugs	5	(5)
Total	99	(100)

was considered positive if at least two of the three major bands—gp160/120, gp41, and p24—were seen (17).

## RESULTS

The average age of the study population was 21 years, within a range of 14 to 32 years. As Table 1 indicates, males comprised 90% of the population—there being 89 males, including four homosexual/bisexual patients. All 99 of the patients were intravenous cocaine abusers, and 10% were also intravenous abusers of morphine, heroin, or other drugs (Table 2).

The subjects' serologic markers related to hepatitis A and B indicated that 62 had acute hepatitis B, 25 had chronic hepatitis B, 10 had hepatitis non-A non-B, and two had hepatitis A (Table 3). Antibodies against the delta agent were detected in five (8%) of the acute cases with hepatitis B and in four (16%) of the chronic cases with hepatitis B (Table 4).

The overall prevalence of HIV-1 anti-

**Table 3.** Types of hepatitis associated with particular serologic markers and the numbers of study subjects classified as having those various types.

Type of hepatitis infection and status	Serologic markers	Study subjects	
		No.	(%)
B, acute <sup>a</sup>	HBsAg (+) and anti-HBc IgM (+)	62 <sup>a</sup>	(63)
B, chronic <sup>b</sup>	HBsAg (+) and anti-HBc (+)	25 <sup>b</sup>	(25)
A, acute	anti-HA IgM (+)	2	(2)
Non-A non-B	HBsAg (-), anti-HBc (-), and anti-HA IgM (-)	10	(10)
Total		99	(100)

<sup>a</sup> Including five cases of delta hepatitis (see Table 4).

<sup>b</sup> Including four cases of delta hepatitis (see Table 4).

**Table 4.** Cases of delta hepatitis among the study subjects, with and without accompanying HIV infection.

Type of case	No. with HDV / No. with HBV	% HBV-positive subjects with delta antibody	Study subjects with HIV-1 and delta antibodies	
			No. with both / No. with delta antibody	
Chronic	4 / 25	16	0/4	
Acute	5 / 62	8	4/5	
Total	9 / 87	10	4/9	

bodies found in the study patients was 47%. More specifically, 47% of the patients with acute hepatitis B tested positive for HIV-1, as did 56% of those with chronic hepatitis B and 40% of those with non-A non-B hepatitis. No HIV-1 antibodies were detected in the two subjects with hepatitis A (Table 5). Likewise, no HIV-1 antibodies were detected in the four subjects with chronic hepatitis B and anti-delta antibodies, but they were found in four of the five subjects with

acute hepatitis B and anti-delta antibodies (see Table 4).

The prevalence of HIV-1 did not differ greatly with sex, HIV-1 antibodies being found in 47% of the males and 50% of the females. Two of the four male homosexual/bisexual patients yielded positive serologic results for the virus.

The duration of drug addiction could only be established with reasonable certainty for 41 of the 99 study subjects. No correlation was found between their length of addiction and the prevalence of HIV-1 antibodies (Table 6).

At least 37 of the 47 patients seropositive for HIV had never traveled abroad and so must have acquired the infection in Argentina. Eight subjects could have acquired the infection in Brazil and two in Bolivia.

Thirty-five percent of the patients studied said they drank alcoholic beverages and indicated that they consumed over 80 g of ethanol daily. However, no correlation was found between this level of drinking and the prevalence of HIV-1 infection (Table 7).

**Table 5.** The prevalence of HIV-1 antibodies observed among the 99 study subjects, grouped according to the type of hepatitis diagnosed.

Type of hepatitis and status	No. of study subjects	Study subjects with antibodies to HIV-1	
		No.	(%)
B, acute	62 <sup>a</sup>	29	(47)
B, chronic	25 <sup>b</sup>	14	(56)
A, acute	2	0	(0)
Non-A non-B	10	4	(40)
Total	99	47	(47)

<sup>a</sup>Including five cases of delta hepatitis.

<sup>b</sup>Including four cases of delta hepatitis.

**Table 6.** HIV-1 seroprevalences in 41 study subjects experiencing drug addiction for different lengths of time.

Length of addiction (years)	No. of study subjects	% HIV-1 seropositive
<1	19	47
1-2	9	55
>2	13	53
Total	41	

## DISCUSSION AND CONCLUSIONS

The prevalence of HIV-1 infection (47%) found among the study subjects was higher than the 22% prevalence detected between July and October 1987 among I.V. drug abusers attending two Buenos Aires rehabilitation clinics (13). However, the latter prevalence increased to 38% when only those I.V. drug abusers

**Table 7.** HIV-1 seroprevalences found among study subjects said to consume over 80 g of ethanol per day and other study subjects.

	Study subjects with daily alcohol consumptions of:				Total	
	≤ 80 g ethanol		> 80 g ethanol			
	No.	(%)	No.	(%)	No.	(%)
HIV-1 (+)	29	(62)	18	(38)	47	(100)
HIV-1 (-)	35	(67)	17	(33)	52	(100)
Total	64	(65)	35	(35)	99	(100)

carrying hepatitis B markers were included.

Despite the preponderance of males among the 99 patients in our study, no marked variation in the seroprevalence of HIV-1 was observed between the sexes.

The youth of our hepatitis-positive study subjects was noteworthy, the subjects' average age being 21 years. However, this situation is comparable to that found in other groups of Argentine I.V. drug abusers, which have typically been comprised mainly of youths around 20 years of age (13). A third of the patients admitted daily alcohol consumption exceeding 80 g of ethanol per day, which is why a transaminase level 10 times higher than normal was required for clinical assignment to that group of patients with some type of viral hepatitis (11). However, no difference was found between the seroprevalences of HIV-1 antibodies among study subjects who consumed over 80 g of ethanol per day and those who did not.

The high percentage of study subjects with hepatitis B (88%) appears reasonable for hepatitis-afflicted I.V. drug abusers in Argentina, as does the low percentage (2%) with hepatitis A (18-20).

There was not any great variation in the seroprevalences of HIV-1 antibodies among study subjects with different hepatitis markers. Specifically, HIV-1 infection was detected in 47% of the 62 subjects with acute hepatitis B infections (including five with the delta marker), in 56% of the 25 subjects with chronic hepa-

titis B infections (including four with the delta marker), and in 40% of the 10 subjects with non-A non-B hepatitis. These findings are consistent with those of Muñoz Domínguez and colleagues (21), who found a significantly lower seroprevalence of HIV-1 in subjects with non-A non-B hepatitis than in those with hepatitis B.

Overall, however, it seems clear that the high prevalence of HIV-1 is related not to the presence of hepatitis B (whether acute or chronic) or non-A non-B hepatitis, but to the route of transmission that their agents share with HIV-1. This is corroborated by a low incidence of HIV antibodies found among nonaddicts and nonintravenous drug addicts positive for HBsAg (22).

Previous studies have reported a direct correlation between HIV prevalence and the length of drug addiction. In our case no correlation was found, perhaps because of the sample's small size (the duration of addiction being known in only 41 cases) and because very few of our subjects had been drug addicts for more than five years. However, some investigators have maintained that acquisition of hepatitis B virus and HIV generally takes place early, during the first two years of drug addiction, and that the prevalences of their markers do not rise notably thereafter (23).

The 10% prevalence of anti-delta antibodies among the 87 study subjects with hepatitis B infections deserves comment, because Argentina is regarded as nonen-

demic for the delta virus. For example, Fay and colleagues found anti-delta antibodies in only 1.8% of 340 Argentine subjects with hepatitis B infections who were not I.V. drug addicts (24). Delta hepatitis was also found to be uncommon in a population of HIV-seropositive I.V. drug abusers in the United States (25). On the other hand, it has been postulated that HIV infection could reactivate both hepatitis B virus and the delta agent (26). (It is known that HIV affects the immune response to hepatitis B virus, and it may prolong productive replication of this virus—27).

HIV-1 antibodies were detected in four of the five subjects with acute hepatitis who were coinfecting with hepatitis B virus and the delta agent; but there was no evidence of HIV-1 infection in the four similarly coinfecting study subjects with chronic hepatitis B. With I.V. drug addiction being on the increase in Argentina, the results of this research presage a significant increase in the delta agent's prevalence in our country in the immediate future.

Overall, the results of this study are noteworthy because they serve to affirm a high incidence of hepatitis B among I.V. drug abusers with hepatitis, to indicate a prevalence of associated delta agent infection significantly higher than that found by previous studies in Argentina, and to demonstrate a high prevalence (47%) of concomitant HIV-1 infection within the study population.

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