

Brief Report

SIMULTANEOUS TRANSMISSION OF HUMAN IMMUNODEFICIENCY VIRUS AND HEPATITIS C VIRUS FROM A NEEDLE-STICK INJURY

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HUMAN immunodeficiency virus type 1 (HIV) and hepatitis C virus (HCV) are blood-borne viruses that pose occupational hazards to health care workers exposed to the blood of infected patients. As of June 1996, 51 documented and 108 possible cases of occupationally acquired HIV infection had been reported to the Centers for Disease Control and Prevention (CDC).¹ The estimated risk of acquiring HIV infection after percutaneous exposure to blood from an HIV-infected patient is 0.3 percent.²

Recommendations for follow-up after occupational exposure to HIV-infected blood include HIV-antibody testing at the time of exposure and periodically for at least six months thereafter.³ Testing for HIV antibody for more than six months after exposure is not routinely recommended, regardless of whether postexposure prophylaxis is used.³

The risk of transmission of HCV to health care workers has not been well defined.⁴ Estimates of the risk of transmission after percutaneous exposure to blood positive for anti-HCV antibody (anti-HCV) range from 0 to 10 percent.⁵⁻¹⁰

We document an infection with both HIV and HCV that a health care worker acquired simultaneously from a single source. Seroconversion to HIV was detected with commercially available assays between 8 and 9½ months after exposure, and seroconversion to HCV occurred between 9½ and 13½

months after exposure. These times to seroconversion are unusually long for both viruses. The clinical course of the health care worker was remarkable for rapid progression to hepatic failure and death.

CASE REPORT

In July 1990, a 48-year-old health care worker in good health sustained a deep injury with a blood-contaminated needle while performing phlebotomy on a patient with the acquired immunodeficiency syndrome (AIDS). Blood also spilled from the collection tube into the spaces between the cuffs of the health care worker's gloves and her wrists and onto her hands, which were chapped with open cracks. Immediately after the incident, the worker removed the gloves and washed her hands.

The patient had a history of injection-drug use. HIV infection had been diagnosed in 1987, and *Pneumocystis carinii* pneumonia in December 1989. At the time of the exposure, the patient was receiving zidovudine therapy, was not recognized as having HCV infection, and had no clinical evidence of liver disease. In March 1991, the CD4 T-lymphocyte count was 32 cells per cubic millimeter.

The health care worker reported no behavioral or transfusion-related risk factors for HIV infection and denied having had any sexual partners during the previous two years. She was not exposed again to blood or body fluids from the patient. Her clinical course and corresponding laboratory test results are summarized in Figure 1.

The health care worker declined zidovudine prophylaxis. No base-line testing for anti-HCV was done because the source patient was not initially identified as HCV-infected. Eight months after the incident, the worker reported low-grade fever, chills, myalgia, nausea, vomiting, diarrhea, sweating, headache, and loss of appetite. Her temperature was 38.2°C, hepatic tenderness was noted, and her serum aminotransferase levels were elevated (Table 1). The white-cell count was 3500 per cubic millimeter, with a differential count of 7 percent band forms, 32 percent segmented forms, 36 percent lymphocytes, 14 percent atypical lymphocytes, 8 percent monocytes, and 3 percent basophils. She was admitted to the hospital with a diagnosis of dehydration and acute hepatitis. Serum was negative for IgM antibody to hepatitis A virus, IgM antibody to hepatitis B virus core antigen, and anti-HCV. Serologic tests for other infectious agents, including Epstein-Barr virus, cytomegalovirus, and leptospira species, were negative. The erythrocyte sedimentation rate and tests for antinuclear antibodies and cold agglutinins were normal. Five days after admission, her symptoms resolved.

Two months later (10 months after exposure), fever (temperature, 38.8°C), photophobia, and a diffuse pruritic rash with dryness of lips and mouth, which was diagnosed as erythema multiforme, developed. Serum obtained 11 months after exposure was positive for anti-HIV antibodies by enzyme immunoassay, and the result was confirmed by Western blotting. Table 2 shows the results of HIV-antibody testing by enzyme immunoassay for controls and all specimens tested at the hospital. Specimens reported as negative (those obtained six weeks, seven months, and eight months after exposure) had optical densities well below the values for positive controls. The health care worker had persistently abnormal serum aminotransferase levels; 16 months after exposure, a test ordered by her health care provider was positive for anti-HCV, and a diagnosis of chronic HCV infection was made (Table 1).

Twenty-one months after exposure, the health care worker's CD4 T-lymphocyte count was 414 cells per cubic millimeter, and her platelet count was 31,000 per cubic millimeter. HIV-induced thrombocytopenia was diagnosed, and therapy with zidovudine was started. Interferon therapy for chronic HCV infection was started but could not be continued because of thrombocytopenia. Three months later, the health care worker presented with hematemesis; endoscopy revealed esophageal varices. Eighteen months after the documented seroconversion to HIV and 28 months af-

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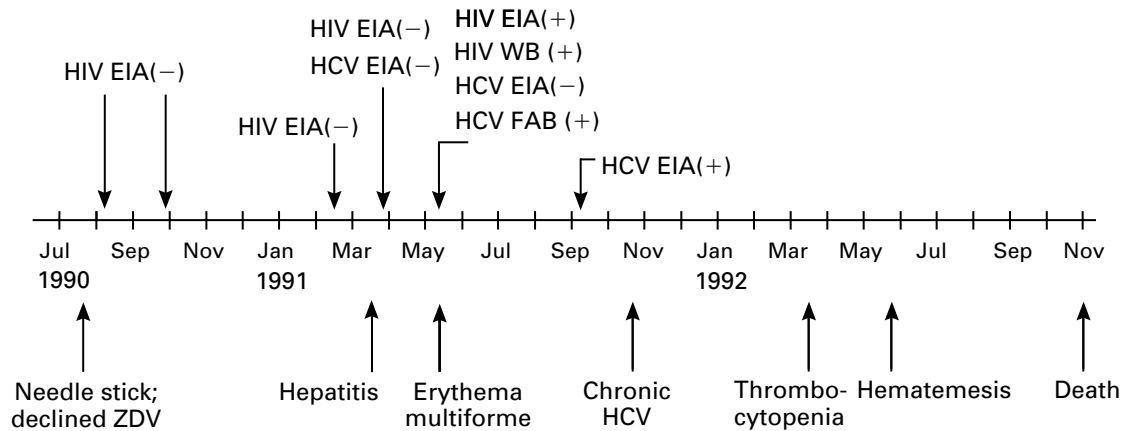


Figure 1. Clinical Course of a Health Care Worker with Percutaneous Exposure to HIV and HCV. HIV denotes human immunodeficiency virus, EIA enzyme immunoassay, ZDV zidovudine, HCV hepatitis C virus, WB Western blotting, and FAB fluorescent-antibody blocking assay.

TABLE 1. LABORATORY FINDINGS IN A HEALTH CARE WORKER WITH PERCUTANEOUS EXPOSURE TO HIV AND HCV.*

TIME	ALT	AST	PLATELETS	CD4	ASSAY FOR ANTI-HIV	ASSAY FOR ANTI-HCV
	U/liter		× 10 ⁻³ /ml	cells/mm ³		
4 mo before exposure	29	28				
Exposure					Negative†	
6 wk					Negative†	
7 mo					Negative†	
8 mo	1793	1209	138		Negative†	Negative‡
9½ mo	724	672	149		Positive§	Negative¶
11 mo	53	54			Positive	
12 mo	131	99	152	1562		
13½ mo						Positive**
14 mo	961	757	136			Positive‡
16 mo	639	1088	100			Positive††
19 mo	147	436	96	568		
21 mo	186	514	31	414		
23 mo	291	591	53	560		
24 mo	221	518	43			
28 mo				736		

*HIV denotes human immunodeficiency virus type 1, HCV hepatitis C virus, ALT alanine aminotransferase, and AST aspartate aminotransferase.

†The assay was HIVAB HIV-1 EIA, Abbott Laboratories, Abbott Park, Ill.

‡The assay was Abbott HCV EIA 1.0, Abbott Laboratories.

§The assays were HIV EIA, Genetic Systems, Portland, Oreg., and HIV-1 Western blot, Cambridge Biotech, Worcester, Mass.

¶The Abbott HCV EIA 2.0, Abbott Laboratories, was used. However, the sample tested positive for antibody to native HCV antigen by fluorescent-antibody blocking assay.¹¹

||The assays used were the HIVAB HIV-1 EIA, Abbott Laboratories, and the Novapath HIV-1 immunoblot, Bio-Rad, Hercules, Calif.

**The assays used were the Abbott HCV EIA 2.0 and the Matrix HCV immunoblot, Abbott Laboratories.

††The assay used was the Ortho HCV ELISA test system; Ortho Diagnostics, Raritan, N.J.

TABLE 2. RESULTS OF HIV ENZYME IMMUNOASSAY OF SERUM FROM THE HEALTH CARE WORKER, WITH CONTROL AND CUTOFF VALUES.*

TIME	NEGATIVE CONTROL	POSITIVE CONTROL	PATIENT'S SERUM	CUTOFF VALUE
				optical density
Exposure	0.028	1.234	0.017	0.151
6 wk	0.025	0.625	0.026	0.088
7 mo	0.039	1.282	0.031	0.167
8 mo	0.054	1.031	0.030	0.157
11 mo	0.066	1.079	>2.200	0.174
11 mo†	0.080	1.049	>2.200	0.185

*The assay was HIVAB HIV-1 EIA, Abbott Laboratories, Abbott Park, Ill.

†This was a repeated test.

ter the needle stick, hepatic coma and progressive renal failure developed, and she died. Postmortem examination showed micronodular cirrhosis of the liver without evidence of any opportunistic infection or cancer.

Stored serum obtained from the health care worker was retrospectively tested at the CDC (Table 1). Serum obtained 9½ months after exposure was positive for HIV antibodies according to enzyme immunoassay and Western blotting. Anti-HCV was not detected by commercial enzyme immunoassay. Serum antibody to native HCV antigen, however, was detected on the basis of inhibition of the binding of fluorescently labeled HCV (fluorescent-antibody blocking assay).¹¹ Specimens obtained from both the source patient and the health care worker 13½ months after exposure were positive for anti-HCV by enzyme immunoassay and supplemental anti-HCV immunoblot assay. Both serum samples from the health care worker had normal immunoglobulin levels and normal results on serum protein electrophoresis.

The strains of HIV and HCV infecting the source patient and the health care worker were compared after amplification by the polymerase chain reaction (PCR) and genetic sequencing.¹²⁻¹⁵ For HIV, viral DNA was amplified from peripheral-blood mononuclear cells obtained from the health care worker and the source patient 13½ months after exposure. The *env* gene was amplified by nested PCR, and the products were cloned.¹⁵ Fifteen clones were selected from both the health care worker and the source patient. A 345-base-pair segment encompassing the C2V3 domain of the *env* gene was sequenced, and phylogenetic analysis was performed.¹⁶

When they were analyzed in relation to sequences of other published HIV reference strains, clones from the health care worker and the source patient were found to be closely related to each other, as indicated by a significant 91 percent bootstrap value at the node leading to all clones (Fig. 2). The bootstrap value is a statistical measure of the likelihood that the clones from the source patient and the health care worker represent highly related variants of HIV. The high degree of relatedness was also evident from the comparison of cloned sequences from the source patient and the health care worker, which showed a low degree (3.7 percent) of genetic difference.

For HCV comparisons, HCV was isolated from serum obtained from the health care worker 9½ and 13½ months after exposure and from the source patient 13½ months after exposure, and it was amplified as previously described.^{13,14,17} PCR amplification and sequencing of 150 bases within the highly conserved 5' untranslated region of the three HCV strains revealed that the sequences were identical and were related to genotype 1.¹⁸ The sequences of 200 bases within the NS5 region were evaluated,

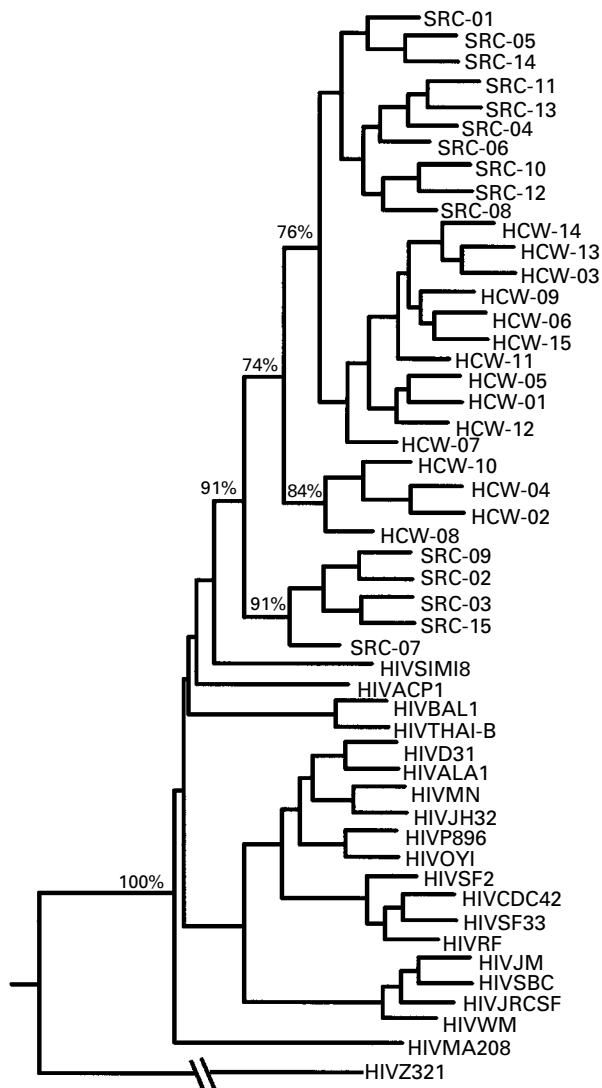


Figure 2. Phylogenetic Analysis of HIV Samples Based on C2V3 Sequence.

SRC denotes variants isolated from the source patient, HCW variants isolated from the health care worker, and HIVZ321 an outgroup reference strain. Other HIVs denote HIV subtype B reference strains. Numbers at the nodes are the bootstrap values (see text).

and the viruses were identified as genotype 1b. These sequences differed by only 0.5 percent when compared with one another, providing further evidence of transmission between the source patient and the infected health care worker.

DISCUSSION

Several features of this health care worker's occupationally acquired illness are unusual. Signs and symptoms consistent with acute HCV infection appeared eight months after exposure, suggesting an unusually long incubation period. The time from exposure to anti-HCV seroconversion was also un-

usually long. In previous reports of HCV transmission by percutaneous injury, the time to seroconversion ranged from three to eight months after exposure.^{8,10,19} The rapid progression to hepatic failure and death in this patient is remarkable. In one retrospective review of patients with transfusion-associated hepatitis C, the mean time to the development of cirrhosis after infection was 20 years.²⁰ The time to HIV seroconversion in this patient was unusually long, and it is one of the longest reported to the CDC. It is not known whether current, more sensitive versions of tests for HIV and HCV antibodies might have been able to detect seroconversion earlier in this health care worker.

The reasons for the unusual clinical and laboratory features of this health care worker's illness are unclear. One possibility is immune dysfunction with delayed antibody response. However, she was previously healthy, without a history of recurrent infection, and the results of serum protein electrophoresis were normal. Therefore, a preexisting immunodeficiency is unlikely. The course may have been related to the simultaneous acquisition of the two infections. There is evidence of pathogenic interaction between the two viruses. The risk of maternal-fetal transmission of HCV may be increased in women who are also HIV-infected,²¹⁻²³ perhaps because of an increased load of HCV.²⁴ In HCV-infected patients with hemophilia, progressive liver disease was seen only in those also infected with HIV.²⁵ In another study, the HCV load was higher in patients with HIV coinfection than in those with HCV infection alone.²⁶ One report suggested that HCV transmission may be more likely if the source patient has dual infection.⁹

A Public Health Service interagency working group on the management of occupational exposure to HIV considered this case as part of a review of available data on the length of the HIV seroconversion window. The group did not recommend routine HIV serologic follow-up beyond six months after exposure, because prolonged follow-up would only rarely detect a new infection and would unnecessarily prolong the anxiety of the exposed health care worker³ (and Bell D: personal communication). In the case of simultaneous occupational exposure to HIV and HCV or in the event of clinical symptoms or signs of infection more than six months after exposure, evaluation for late seroconversion may be needed. The possible pathogenetic interactions between HIV and HCV warrant further study.

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