HEPATITIS B AND HEPATITIS C IN EMERGENCY DEPARTMENT PATIENTS

GABOR D. KELEN, M.D., GARY B. GREEN, M.D., ROBERT H. PURCELL, M.D., DANIEL W. CHAN, PH.D., BAHJAT F. QAQISH, M.D., PH.D., KEITH T. SIVERTSON, M.D., AND THOMAS C. QUINN, M.D.

Abstract *Background.* Infections with hepatitis B virus (HBV), hepatitis C virus (HCV), and the human immunodeficiency virus type 1 (HIV-1) are common in inner-city populations, but their frequency and interrelations are not well established.

Methods. During a six-week period, excess serum samples were collected, along with information on risk factors, from all adult patients presenting to an inner-city emergency department. The samples were assayed for hepatitis B surface antigen (HBsAg) and antibodies to HCV and HIV-1.

Results. Of the 2523 patients tested, 612 (24 percent) were infected with at least one of the three viruses. Five percent were seropositive for HBV, 18 percent for HCV, and 6 percent for HIV-1. HCV was found in 145 of the 175 intravenous drug users (83 percent), 36 of the 171 transfusion recipients (21 percent), and 5 of the 24 homosexual men (21 percent). Among black men 35 to 44 years of age, the seroprevalence of HCV was 51 percent. HBsAg was present in 9 percent of those whose only identifiable risk was possible heterosexual exposure. At least one viral marker was found in about 30 percent of the patients who were actively bleeding or in whom procedures were performed. Testing for HIV-1 alone would have failed to identify 87 percent of the patients infected with HBV and 80 percent of those infected with HCV.

Conclusions. In a population of patients in an inner-city emergency room, HBV, HCV, and HIV-1 are all highly prevalent. However, routine screening for HIV-1 alone would identify only a small fraction of the patients who pose risks of severe viral infections, including HBV and HCV, to providers. (N Engl J Med 1992;326:1399-404.)

IN addition to human immunodeficiency virus type 1 (HIV-1), hepatitis B virus (HBV) and hepatitis C virus (HCV) are major sources of public health concern. Approximately 25 percent of adults infected with HBV become ill with jaundice, and of the 6 to 10 percent with acute infections who become carriers, about a quarter progress to chronic active hepatitis.[1] In a substantial proportion cirrhosis or primary hepatocellular carcinoma develops. HCV is considered to be the chief etiologic agent for both parenterally transmitted[2-4] and sporadic[5-7] non-A, non-B hepatitis. Although HCV infection is usually not severe and is often asymptomatic, chronic hepatitis develops in at least 50 percent of those infected, and at least 10 percent will die of associated complications.[8] The presence of antibody to HCV is particularly associated with chronic liver disease in persons with post-transfusion non-A, non-B hepatitis,[9] and it may also be associated with more severe alcoholic liver disease[10,11] and the development of hepatocellular carcinoma.[10,12-14]

HBV, HCV, and HIV-1 share modes of transmission and are relatively prevalent among certain population groups. However, their seroprevalences and interrelations in a general inner-city population of patients have not been described. Also, since parenteral transmission appears relatively efficient for these viruses, percutaneous exposure represents an occupational risk to health care providers. Routine testing of patients for HIV-1 has recently been advocated as a means of increasing provider vigilance and reducing occupational exposures.[15,16] However, a strict focus on routine HIV-1 testing may not identify patients with other transmissible blood-borne infections, such as HBV and HCV.

We previously reported a high seroprevalence of HIV-1 infection (6.0 percent) among patients in our emergency department.[17] We now describe the seroprevalence and epidemiologic characteristics of HCV and HBV among 2523 patients in the emergency department and examine the interrelations among active HCV, HBV, and HIV-1 infections. We also assess the potential value of routine testing of patients only for HIV-1 in this setting as a means of identifying those who pose a risk of HBV or HCV to providers.

METHODS

The facility and study design have been described previously in a report on the seroprevalence of HIV-1 in our emergency department population.[17] Briefly, for six consecutive weeks from June through August 1988, excess serum was retained from all patients 15 years of age or older who presented to the emergency department at Johns Hopkins Hospital and had blood drawn. Serum samples and data were collected prospectively with a procedure in which the patient's identity was not linked with the sample. Serum specimens and corresponding data-collection sheets were labeled with preassigned study numbers that did not contain any patient identifiers. Data were collected 24 hours a day during the patients' visits by study investigators who were not involved in the patients' care. The serum samples were analyzed for antibody to HIV-1[17] and for hepatitis B surface antigen (HBsAg), and subsequently, when assays for HCV became available, for antibody to HCV. The study design was approved by the institution.

Data on demographics, clinical condition, procedures performed, observed exposures of providers to the patient's blood and body fluids, and risk factors were collected for each patient. At the time of the study, it was routine policy in the emergency department to inquire about risks for blood-borne infections, with HIV-1 transmission used as a model. Thus, the risk factors ascertained were any history within the past 10 years of intravenous drug use, homosexual or bisexual activity in men, receipt of blood products, or heterosexual activity with a partner who had any of the foregoing risk factors. The risk factors were determined by a study investigator

From the Divisions of Emergency Medicine (G.D.K., G.B.G., K.T.S.) and Infectious Disease (T.C.Q.), Johns Hopkins University School of Medicine, and the Department of Laboratory Medicine (D.W.C.), Johns Hopkins Hospital, Baltimore; the Department of Biostatistics (B.F.Q.), University of North Carolina, Chapel Hill; and the Laboratory of Infectious Diseases (R.H.P.), and the Laboratory of Immunoregulation (T.C.Q.), National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Md. Address reprint requests to Dr. Kelen at the Department of Emergency Medicine, Marburg B186, Johns Hopkins Hospital, 600 N. Wolfe St., Baltimore, MD 21205.

Supported by grants from the W.M. Keck Foundation and the Emergency Medicine Foundation.

(not involved in the patient's care) who interviewed each patient directly; the interview was supplemented by a review of the patient's chart. The risk factors were categorized as being present, absent (the category that was used when a patient denied having a risk factor), or of unknown status. The last category was used in the case of patients for whom no risk factors were found but whose medical condition precluded a full assessment of risk. Unprotected exposures of providers to patients' blood and body fluids were monitored prospectively by direct observation, and this information was supplemented in interviews with the providers.

Serologic Analysis

Serum samples were frozen and stored at −70° C. They were each evaluated by enzyme-linked immunosorbent assay (ELISA) for antibodies to HIV-1 (Organon–Teknika, Charleston, S.C.), and all repeatedly reactive specimens were analyzed by Western blotting for reactivity with HIV-1 protein (Dupont, Wilmington, Del.). Specimens with multiple antibody bands reactive to p24, p31, and gp41 or gp120/160 were considered seropositive.

Antibody to HCV was detected by the first-generation assay Ortho HCV ELISA Test System (Ortho Diagnostics, Raritan, N.J.).[6] All samples repeatedly reactive were tested further by an HCV dot blot immunoassay (Matrix HCV, Abbott Laboratories, Abbott Park, Ill.). The Matrix HCV antigen test panel consists of recombinant antigens that represent three nonoverlapping regions of the HCV genome: C100 (a nonstructural gene 4 product), 33c (a nonstructural gene 3 product), and core (viral nucleocapsid). Samples were considered positive if two or more distinct antigens were reactive, negative if there were no reactive antigens, and indeterminate if the reactivity pattern did not meet either of these criteria.[18]

Samples reactive for antibodies to HCV were also analyzed by the recombinant immunoblot assay system (RIBA-1, Ortho Diagnostics).[19] Samples were considered positive if both the C100-3 and 5-1-1 bands were present. A sample was considered indeterminate if there were bands present but the criteria for reactivity were not met or if the control band of superoxide dismutase was reactive along with the C100-3 band, the 5-1-1 band, or both.

HBsAg was detected with the NML ELISA (Organon–Teknika, Durham, N.C.). All repeatedly reactive specimens were considered positive for HBsAg.

Data Analysis

Comparisons were made by the chi-square test for proportions and the test of independence, Fisher's exact test, or Student's t-test. Seroprevalence rates specific to age and race were analyzed by grouping the patients in 10-year age intervals and calculating the age-specific seroprevalence rate for each interval. These rates were then plotted at the midpoints of the intervals. Seroprevalence curves were obtained by smoothing the original ungrouped data with a smoothing technique.[20] Unlike the method used in our previous studies,[17,21] risk factors were not ordered hierarchically, because the resulting hierarchy may be different for each type of viral infection, rendering comparison difficult. Thus, risk factors were categorized according to whether the patient had a single risk factor, had multiple risk factors, acknowledged no risk factors, or had no identified risks but incomplete ascertainment of risk factors. Multivariate logistic-regression analysis was performed to determine which characteristics of patients were independently associated with each viral infection.[22] The method used also allowed the estimation of pairwise association among the three markers after adjustment for the effects of covariates on each.[22]

Results

There were 5229 visits by patients to the emergency department during the study. Among these patients, 2613 had blood drawn, but 90 patients had insufficient excess serum samples for all analyses to be completed. Thus, there were 2523 patients in the study sample. Of these, 1216 (48 percent) were men, and 1307 (52 percent) were women. There were 1947 blacks (77 percent), 559 whites (22 percent), and 17 members of other races (<1 percent). Thirty-three percent of the patients were admitted to the hospital.

Seroprevalence of Viral Markers

Six hundred twelve patients (24 percent) had at least one viral marker. There were 458 serum samples positive for HCV (18 percent), 129 positive for HBsAg (5 percent), and 152 positive for HIV-1 (6 percent) (Table 1). Of the patients with HIV-1 infection only, 57 (38 percent) knew they were infected. Only 4 of those with HBsAg (3 percent) and 16 of those with HCV (3 percent) presented with clinical evidence of possible liver disease (jaundice, hepatomegaly, or ascites).

The mean (±SD) age of the patients was 43±19 years, and the ages of those with HBsAg, HCV, and HIV-1 were 41±18, 37±13, and 34±8 years, respectively. Race- and sex-specific curves of seroprevalence plotted against age are shown in Figure 1. The highest seroprevalence rate for HCV (51 percent) was found among black men 35 to 44 years of age. In this group, 58 percent were infected with at least one of the three viruses. Among whites, the highest rate of HCV seroprevalence (21 percent) was also found among men 35 to 44 years old. The highest seroprevalence rate for HBsAg was found among black men 55 to 64 years old (10 percent) and over 84 years old (11 percent) (Fig. 1). Logistic-regression analysis revealed that persons 25 to 34, 35 to 44, and 55 to 64 years old had significantly higher seroprevalence rates for HCV than those over 64 years old (Table 2). The prevalence of HBsAg did not vary significantly with age.

In 91 specimens there was evidence of infection with both HCV and HIV-1 (odds ratio, 8.1; 95 percent confidence interval, 5.8 to 11.5), and in 17 there were infections with both HIV-1 and HBsAg (odds ratio, 2.5; 95 percent confidence interval, 1.5 to 4.3). The hypothesis of independent distributions was rejected for each of these two relations ($P<0.001$). This hypothesis could not be rejected in the case of the 30 persons infected with both HCV and HBsAg (odds ratio, 1.4; 95 percent confidence interval, 0.9 to 2.1; $P = 0.12$). The multivariate logistic-regression model revealed that once other covariates were taken into account, none of the three associations were statistically significant (Table 2). Although more coinfections occurred than would have been predicted by the seroprevalence rates observed, infections with HBsAg and HCV each occurred more often in the absence of other infections. A total of 460 patients (18 percent) had either HCV or HBsAg without concurrent HIV-1 infection. Testing for HIV-1 antibody alone would have missed 367 of 458 patients with HCV infection (80 percent) and 112 of 129 carriers of HBsAg (87 percent). Overall, testing for HIV-1 would have failed

Table 1. Seroprevalence of Viral Markers among 2523 Patients in the Emergency Department, According to Risk Factors.

Risk Factor	No. of Patients	Viral Marker			
		anti-HCV	HBsAg	anti-HIV-1	any
		no. (%) positive			
At least one	540	274 (51)	35 (7)	120 (22)	330 (61)
Intravenous drug use	175	145 (83)	10 (6)	47 (27)	153 (87)
Homosexual sex	24	5 (21)	4 (17)	16 (67)	19 (79)
Blood products	171	36 (21)	8 (5)	8 (5)	47 (28)
Heterosexual exposure to partner at risk	47	3 (6)	4 (9)	4 (9)	11 (23)
More than one risk factor	123	85 (69)	9 (7)	45 (37)	100 (81)
None acknowledged	726	63 (9)	34 (5)	11 (2)	98 (14)
None known	1257	121 (10)	60 (5)	21 (2)	184 (15)
All*	2523	458 (18)	129 (5)	152 (6)	612 (24)

*Represents the sum of the values for at least one risk factor, none acknowledged, and none known.

to identify 460 of 629 patients (73 percent) with at least one infection other than HIV-1.

Seroprevalence According to Risk Factors

Seroprevalence rates of HCV, HBsAg, and HIV-1 in the population stratified according to risk factor are shown in Table 1. Intravenous drug users had particularly high rates of viral infection, particularly with HCV (83 percent). Persons with homosexual activity as their only risk factor had relatively high rates of all three viral markers, with 79 percent having evidence of at least one viral infection. Relatively high rates of infection were also found among those whose only acknowledged risk factor was heterosexual exposure; at least one marker was found in 23 percent. Even the group of those with no identified risks had relatively high rates of infection with each virus. Multivariate logistic regression revealed that the only risk independently associated with HBsAg was homosexuality, whereas both intravenous drug use and the receipt of blood products were associated with HCV (Table 2).

We examined whether the presence of HIV-1 increased the likelihood of coinfection with either HCV or HBsAg for patients in the various risk categories. No increase in the prevalence of either virus was found among those in single-risk categories ($P>0.2$). The regression analysis that addressed these associations in those with multiple risk factors had similar results (Table 2).

Potential Exposure of Health Care Providers to Viral Infection

The incidence of unprotected exposure to patients' blood or body fluids was assessed for 98 percent of the patients. Situations that placed providers at increased risk occurred in significant numbers (Table 3). Routine testing only for HIV-1 would have missed 74 to 88 percent of infections with HCV or HBsAg among patients posing particular risks of exposure to providers. Of the unprotected (nonpercutaneous) exposures of providers to infected blood or body fluids, 88 percent and 75 percent, respectively, involved viruses other than HIV-1. Routine testing only for HIV-1 would have missed 11 of 14 viral infections (79 percent) among those requiring immediate major surgery. Screening for HBsAg in addition to HIV-1 would still have failed to identify 10 such patients who had HCV infection only (71 percent).

Discussion

We found high seroprevalence rates of HBsAg, HCV, and HIV-1 among the patients in our emergency department in inner-city Baltimore. Nearly 25 percent of the patients were actively infected with at least one of these viruses. Although general serologic surveys of HCV have been undertaken[23,24] and high seroprevalence rates of HCV have been reported among specific risk groups, such as intravenous drug us-

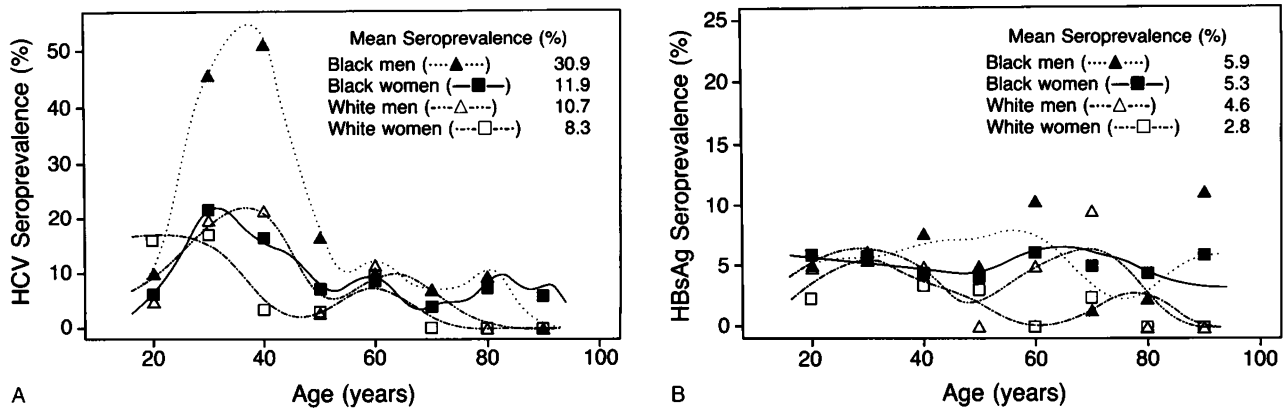

Figure 1. Smoothed Seroprevalence Curves for Antibody to HCV (Panel A) and for HBsAg (Panel B) among 2523 Patients in the Emergency Department.

Values for patients grouped according to 10-year age intervals are plotted at the middle of each interval for comparison with the smoothed curve.

Table 2. Multivariate Logistic-Regression Analysis of Seropositivity for HBsAg and Antibody to HCV among Patients in the Emergency Department.

Characteristic	HBsAg		Anti-HCV	
	Odds ratio (95% confidence interval)	P value	Odds ratio (95% confidence interval)	P value
Age (yr)				
15–24	1.62 (0.65–4.02)	0.30	1.03 (0.49–2.17)	0.93
25–34	1.63 (0.68–3.88)	0.27	3.18 (1.66–6.09)	<0.001
35–44	1.72 (0.70–4.25)	0.24	4.36 (2.28–8.32)	<0.001
45–54	1.14 (0.41–3.20)	0.81	1.10 (0.50–2.42)	0.81
55–64	2.15 (0.94–4.92)	0.07	2.13 (1.06–4.30)	0.03
>64*	1.00	—	1.00	—
Race				
Black	1.50 (0.89–2.50)	0.13	2.03 (1.38–3.00)	<0.001
White*	1.00	—	1.00	—
Sex				
Male	1.09 (0.75–1.59)	0.66	2.00 (1.53–2.61)	<0.001
Female*	1.00	—	1.00	—
Risk factor				
Homosexual sex	4.59 (1.41–14.88)	<0.01	1.56 (0.50–4.87)	0.45
Intravenous drug use	1.05 (0.58–1.86)	0.91	22.40 (15.23–32.95)	<0.001
Receipt of blood products	1.05 (0.58–1.90)	0.88	1.88 (1.24–2.84)	<0.003
Heterosexual sex with partner at risk	1.12 (0.47–2.64)	0.80	0.66 (0.38–1.15)	0.14
None known*	1.00	—	1.00	—
Viral marker†				
Anti-HIV-1	1.84 (0.86–3.92)	0.12	1.73 (0.95–3.17)	0.07
Anti-HCV	1.16 (0.72–1.90)	0.54	—	—

*Reference category.

†Data shown are for the comparison with patients in whom the marker is absent.

ers,[25,26] there are few data on HCV in inner-city populations. The 18 percent HCV seroprevalence rate found in this study represents one of the highest rates reported in a general population of patients. We found that HCV was concentrated among patients 25 to 44 years old, with a particularly high prevalence among minorities, as noted in a previous study.[24]

The seroprevalence of HCV among intravenous drug users (83 percent) was similar to that found by others in the Baltimore–Washington, D.C., area.[25] Among the men who acknowledged homosexual activity as their only risk factor (21 percent), HCV seroprevalence was higher than that suggested by other studies,[3,25,27-29] and this may indicate an increasing spread among this risk group in our area. Although some studies suggest that heterosexual exposure to HCV is not a major risk factor for transmission,[29,30] our data support the findings of others that such transmission can be considerable, even if less efficient than that occurring by other routes.[3,5,27,28,31,32] Still, among those with possible heterosexual exposure as their only risk factor, HCV seroprevalence was comparatively lower than in other risk groups. Heterosexual exposure may have been underdetected, however, and it may thus be responsible for infections found among those with no identified risks.[33] Unreported intravenous drug use may also explain some of these infections, as well as those occurring in other risk groups. Still, the high proportion of patients infected with HCV in whom we did not identify a possible source of exposure (40 percent) was similar to that reported in the literature.[5]

The seroprevalence of HBsAg among our patients (5 percent) was also one of the highest reported for a general population of patients,[34,35] a finding that supports calls for programs of universal vaccination.[36] HBsAg was most commonly found among black men (6 percent), although neither race nor sex was independently associated with it. The seroprevalence of HBsAg among patients in our risk groups was similar to that observed in the Veterans Affairs study conducted near Baltimore.[34]

The issue of routinely testing patients for HIV-1 as a means of identifying those who may pose a risk of infection in an occupational setting has received considerable attention.[15,16] We found, however, that almost 20 percent of our patients had active HBV or HCV infection without concurrent HIV-1 infection. Testing for HIV-1 antibody alone would have missed 367 of all the HCV infections (80 percent) and 112 of those with HBsAg (87 percent). It should be noted that almost a third of the patients who went directly from the emergency department to the operating suite were found to have at least one viral infection, and the vast majority of these (79 percent) would not have been identified by routine screening for HIV-1 alone (Table 3). As we found with HIV-1,[17] patients with HBsAg or HCV cannot be reliably identified on the basis of patient-associated characteristics, risk assessment, or clinical presentation. Clinical condition appears to be the least helpful, since only 3 percent of those with HBsAg and 3 percent of those seropositive for HCV had evidence of liver disease. Given the wide distribution of these viruses in this population, routine HIV-1 testing would be relatively ineffectual as a

Table 3. Potential Exposure of Health Care Providers to Virus from Patients.

Situation	No. of Potential Exposures	Viral Marker				Virus Missed by Routine HIV-1 Testing
		Anti-HCV	HBsAg	Anti-HIV-1	Any	
		number (percent) positive				
Altered consciousness	363	80 (22)	20 (6)	14 (4)	95 (26)	81 (85)
Active bleeding	477	117 (25)	23 (5)	32 (7)	140 (29)	108 (77)
Exposure to patient's blood	32	6 (19)	4 (13)	1 (3)	8 (25)	7 (88)
Exposure to patient's body fluids	17	3 (18)	1 (6)	1 (6)	4 (24)	3 (75)
Patient taken directly to operating suite	44	13 (30)	1 (2)	3 (7)	14 (32)	11 (79)
Major procedures	177	48 (27)	6 (3)	17 (10)	68 (38)	51 (75)
Minor procedures	3962	714 (18)	194 (5)	249 (6)	945 (24)	696 (74)

means of alerting providers to patients who may pose an occupational risk. Adherence to universal precautions remains the best strategy for this purpose.

We chose to assay for antibodies to HIV-1, HCV, and HBsAg because the presence of each of these markers implies the ability to transmit virus.[1,2,4,6,37-40] Thus, some assessment of the potential risk to providers from contact with these viruses could be undertaken. The potential for the exposure of providers and subsequent transmission of viral infection in this setting is considerable (Table 3). During the six weeks of our study, we documented more than 4000 major and minor invasive procedures, and 477 of the patients were actively bleeding. The annual risk of HIV-1 acquisition in an emergency department such as ours, where there is a high potential for exposure to this virus, has been estimated at only 0.026 percent per provider.[41] However, the cumulative risk of occupational acquisition of HIV-1 over the course of a 30-year career in an environment such as ours has been estimated to be 1.4 percent (90 percent confidence interval, 0.2 percent to 14.0 percent) — a figure that is not inconsequential.[42] Consistent adherence to universal precautions would decrease this risk by an estimated 30 percent.[42]

The rate of occupational acquisition of HBV among unvaccinated health care providers may be approximately 50 to 100 percent higher than the rate for HIV-1, since the risk of transmission after percutaneous exposure to HBsAg-positive blood can be as high as 30 percent.[43] The prevalence of markers of HBV infection among unvaccinated providers who come into frequent contact with blood ranges from 15 percent to 30 percent — 3 to 10 times higher than in providers without much contact with blood.[1] Unvaccinated personnel in the emergency department are at particular risk: 30 percent have been shown to have markers for HBV, the highest such rate of any group of providers.[44,45] HBV transmission in the workplace remains a concern despite the availability of a vaccine. Only 50 percent of physicians in the United States[46] and only 42 percent of all providers with responsibilities for patient care[47] are believed to be vaccinated for HBV at this time.

The risk of occupational acquisition of HCV is only now being assessed. However, there have been several cases of such transmission in an occupational setting.[48-50] A recent study reported that acute HCV infection with seroconversion occurred in 3 of 110 providers (2.7 percent) who had documented needle-stick exposures to the blood of patients with antibodies to HCV.[49] Before the advent of HCV assays, there were several reports of occupational transmission of non-A, non-B hepatitis,[51,52] and others have noted that this form of hepatitis appears to be more frequent among providers involved in patient care or those who have laboratory responsibilities than in control populations.[5,27,28]

This study has some limitations. Although we found the seroprevalence of HCV among our patients to be high, we may in fact have underestimated it. The time required for seroconversion can be long,[4,6] and the first-generation screening assay used may have failed to identify some infected patients with low titers of antibodies or with antibodies to other antigens of HCV.[53] The transfusion of blood seronegative for HCV has resulted in the transmission of HCV, with seroconversion in patients who subsequently had post-transfusion non-A, non-B hepatitis.[2]

The data on risk factors should be approached with some caution. In the absence of specific indications, providers rarely evaluate specific risk factors for viral hepatitis in the emergency department. Also, the assessment of other risk factors in such settings is limited, and thus some patients with infections but without identified risks may in fact have engaged in risky behavior or activities.[33] Also, infection rates among members of risk groups presenting in our emergency department may not represent the rates in the population at large. Still, the proportion of members of risk groups who were infected with HCV or HBsAg and in whom no risks were identified was similar to that found in other surveys.[5,25,26,31,32,34]

In summary, this study provides evidence of a high prevalence of presumed infectivity of HCV and HBV in an unselected but well-defined population of patients who also have a high prevalence of HIV-1 infection. The study also provides preliminary evidence that sexual transmission of HCV may be more common than has been previously appreciated. Exposure to HCV, HBV, and HIV-1 in health care settings in the inner city may be considerable without appropriate infection-control procedures. Apart from the clinical sequelae, the acquisition of any of these viruses may prevent providers from continuing to practice their professions,[54] as recent developments attest. We believe that our data demonstrate the inability of routine HIV-1 screening to identify most patients who pose a risk to providers in such settings, and thus underscore the need for rigorous adherence to universal precautions and for continued implementation of HBV vaccination programs.

We are indebted to Richard Kline, M.Sc., of the Laboratory of Immunoregulation, and Doris Wong, B.S., of the Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health; and to David Vallari of Abbott Laboratories, for their assistance with serologic analyses of specimens for antibody to HCV.

References

1. Protection against viral hepatitis: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1990;39:Suppl RR-2:5-22.
2. Esteban JI, González A, Hernández JM, et al. Evaluation of antibodies to hepatitis C virus in a study of transfusion-associated hepatitis. N Engl J Med 1990;323:1107-12.
3. Esteban JI, Esteban R, Viladomiu L, et al. Hepatitis C virus antibodies among risk groups in Spain. Lancet 1989;2:294-7.
4. Alter HJ, Purcell RH, Shih JW, et al. Detection of antibody to hepatitis C virus in prospectively followed transfusion recipients with acute and chronic non-A, non-B hepatitis. N Engl J Med 1989;321:1494-500.

5. Alter MJ, Hadler SC, Judson FN, et al. Risk factors for acute non-A, non-B hepatitis in the United States and association with hepatitis C virus infection. JAMA 1990;264:2231-5.
6. Kuo G, Choo Q-L, Alter HJ, et al. An assay for circulating antibodies to a major etiologic virus of human non-A, non-B hepatitis. Science 1989;244: 362-4.
7. Hopf U, Moller B, Kuther D, et al. Long-term follow-up of posttransfusion and sporadic chronic hepatitis non-A, non-B and frequency of circulating antibodies to hepatitis C virus (HCV). J Hepatol 1990;10:69-76.
8. Dienstag JL. Non-A, non-B hepatitis. I. Recognition, epidemiology, and clinical features. Gastroenterology 1983;85:439-62.
9. Mosley JW, Aach RD, Hollinger FB, et al. Non-A, non-B hepatitis and antibody to hepatitis C virus. JAMA 1990;263:77-8.
10. Nalpas B, Driss F, Pol S, et al. Association between HCV and HBV infection in hepatocellular carcinoma and alcoholic liver disease. J Hepatol 1991;12:70-4.
11. Pares A, Barrera JM, Caballeria J, et al. Hepatitis C virus antibodies in chronic alcoholic patients: association with severity of liver injury. Hepatology 1990;12:1295-9.
12. Sakamoto M, Hirohashi S, Tsuda H, et al. Increasing incidence of hepatocellular carcinoma possibly associated with non-A, non-B hepatitis in Japan, disclosed by hepatitis B virus DNA analysis of surgically resected cases. Cancer Res 1988;48:7294-7.
13. Colombo M, Kuo G, Choo QL, et al. Prevalence of antibodies to hepatitis C virus in Italian patients with hepatocellular carcinoma. Lancet 1989;2:1006-8.
14. Kew MC, Houghton M, Choo QL, Kuo G. Hepatitis C virus antibodies in southern African blacks with hepatocellular carcinoma. Lancet 1990;335: 873-4.
15. Rhame FS, Maki DG. The case for wider use of testing for HIV infection. N Engl J Med 1989;320:1248-54.
16. Angell M. A dual approach to the AIDS epidemic. N Engl J Med 1991; 324:1498-500.
17. Kelen GD, DiGiovanna T, Bisson L, Kalainov D, Sivertson KT, Quinn TC. Human immunodeficiency virus infection in emergency department patients: epidemiology, clinical presentations, and risk to health care workers: the Johns Hopkins experience. JAMA 1989;262:516-22.
18. Vallari DS, Jett BW, Alter HJ, Mimms LT, Holzman R, Shih JW-K. Serologic markers of posttransfusion hepatitis C viral infection. J Clin Microbiol 1992;30:552-6.
19. Weiner AJ, Truett MA, Rosenblatt J, et al. HCV testing in low-risk populations. Lancet 1990;336:695.
20. Watson GS. Smooth regression analysis. Sankhya [A] 1964;26:359-78.
21. Kelen GD, Fritz S, Qaqish B, et al. Unrecognized human immunodeficiency virus infection in emergency department patients. N Engl J Med 1988; 318:1645-50.
22. Liang K-Y, Zeger SL, Qaqish BF. Multivariate regression models and analyses for categorical data. J R Stat Soc [B] (in press).
23. Blood transfusion and the transmission of HCV. In: Proceedings of the First International Symposium on Hepatitis C Virus, Chapter II. Raritan, N.J.: Ortho Diagnostic Systems, 1989.
24. Stevens CE, Taylor PE, Pindyck J, et al. Epidemiology of hepatitis C virus: a preliminary study of volunteer blood donors. JAMA 1990;263:49-53.
25. Donahue JG, Nelson KE, Munoz A, et al. Antibody to hepatitis C virus among cardiac surgery patients, homosexual men, and intravenous drug users in Baltimore, Maryland. Am J Epidemiol 1991;134:1206-11.
26. Williams AE, Dodd RY. The serology of hepatitis C virus in relation to post-transfusion hepatitis. Ann Clin Lab Sci 1990;20:192-9.
27. Alter MJ, Coleman PJ, Alexander WJ, et al. Importance of heterosexual activity in the transmission of hepatitis B and non-A, non-B hepatitis. JAMA 1989;262:1201-5.
28. Alter MJ, Gerety RJ, Smallwood LA, et al. Sporadic non-A, non-B hepatitis: frequency and epidemiology in an urban U.S. population. J Infect Dis 1982;145:886-93.
29. Melbye M, Biggar RJ, Wantzin P, et al. Sexual transmission of hepatitis C virus: cohort study (1981-9) among European homosexual men. BMJ 1990; 301:210-2.
30. Everhart JE, Di Bisceglie AM, Murray LM, et al. Risk for non-A, non-B (type C) hepatitis through sexual or household contact with chronic carriers. Ann Intern Med 1990;112:544-5.
31. Hess G, Massing A, Rossol S, Schütt H, Clemens R, Meyer Zum Büschenfelde K-H. Hepatitis C virus and sexual transmission. Lancet 1989;2:987.
32. Tor J, Llibre JM, Carbonell M, et al. Sexual transmission of hepatitis C virus and its relation with hepatitis B virus and HIV. BMJ 1990;301:1130-3.
33. Liddle C, Crewe EB, Swanson NR, et al. Does hepatitis C virus play a role in "non-viral" chronic liver disease? Med J Aust 1990;153:265-71.
34. Gordin FM, Gibert C, Hawley HP, Willoughby A. Prevalence of human immunodeficiency virus and hepatitis B virus in unselected hospital admissions: implications for mandatory testing and universal precautions. J Infect Dis 1990;161:14-7.
35. Handsfield HH, Cummings MJ, Swenson PD. Prevalence of antibody to human immunodeficiency virus and hepatitis B surface antigen in blood samples submitted to a hospital laboratory: implications for handling specimens. JAMA 1987;258:3395-7.
36. Hepatitis B virus: a comprehensive strategy for eliminating transmission in the United States through universal childhood vaccination: recommendations of the Immunization Practices Advisory Committee (ACIP). MMWR 1991;40:Suppl RR-13:1-25.
37. Evatt BL, Gomperts ED, McDougal JS, Ramsey RB. Coincidental appearance of LAV/HTLV-III antibodies in hemophiliacs and the onset of the AIDS epidemic. N Engl J Med 1985;312:483-6.
38. Johnson RE, Lawrence DN, Evatt BL, et al. Acquired immunodeficiency syndrome among patients attending hemophilia treatment centers and mortality experience of hemophiliacs in the United States. Am J Epidemiol 1985;121:797-810.
39. Farci P, Alter HJ, Wong D, et al. A long-term study of hepatitis C virus replication in non-A, non-B hepatitis. N Engl J Med 1991;325:98-104.
40. Choo Q-L, Kuo G, Weiner AJ, Overby LR, Bradley DW, Houghton M. Isolation of a cDNA clone derived from a blood-borne non-A, non-B viral hepatitis genome. Science 1989;244:359-62.
41. Marcus R, Bell DM, Culver DH, Cooperative Emergency Department Study Group. Frequency of emergency care providers' contact with blood of patients infected with human immunodeficiency virus. Presented at the Annual Meeting of the Society for Academic Emergency Medicine, Minneapolis, May 22, 1990.
42. Wears RL, Vukich DJ, Winton CN, Fluskey LL, MacMath TR, Li S. An analysis of emergency physicians' cumulative career risk of HIV infection. Ann Emerg Med 1991;20:749-53.
43. Guidelines for prevention of transmission of human immunodeficiency virus and hepatitis B virus to health-care and public-safety workers. MMWR 1989;38:Suppl S-6.
44. Jovanovich JF, Saravolatz LD, Arking LM. The risk of hepatitis B among select employee groups in an urban hospital. JAMA 1983;250:1893-4.
45. Dienstag JL, Ryan DM. Occupational exposure to hepatitis B virus in hospital personnel: infection or immunization? Am J Epidemiol 1982;115:26-39.
46. Update on hepatitis B prevention. MMWR 1987;36:353-66.
47. Alexander PG, Johnson R, Williams WW, Hadler SC, White JW, Coleman PJ. Hepatitis B vaccination programs for health care personnel in U.S. hospitals. Public Health Rep 1990;105:610-6.
48. Schlipkoter U, Roggendorf M, Cholmakow K, Weise A, Deinhardt F. Transmission of hepatitis C virus (HCV) from a haemodialysis patient to a medical staff member. Scand J Infect Dis 1990;22:757-8.
49. Kiyosawa K, Sodeyama T, Tanaka E, et al. Hepatitis C in hospital employees with needlestick injuries. Ann Intern Med 1991;115:367-9.
50. Seeff LB. Hepatitis C from a needlestick injury. Ann Intern Med 1991;115: 411.
51. Ahtone J, Francis D, Bradley D, Maynard J. Non-A, non-B hepatitis in a nurse after percutaneous needle exposure. Lancet 1980;1:1142.
52. Mayo-Smith MF. Type non-A, non-B and type B hepatitis transmitted by a single needlestick. Am J Infect Control 1987;15:266-7.
53. Werner AJ, Kuo G, Bradley DW, et al. Detection of hepatitis C viral sequences in non-A, non-B hepatitis. Lancet 1990;335:1-3.
54. Recommendations for preventing transmission of human immunodeficiency virus and hepatitis B virus to patients during exposure-prone invasive procedures. MMWR 1991;40:Suppl RR-8:1-9.