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HEPATITIS C VIRUS IN HEALTH CARE WORKERS

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Overview and Epidemiology

Hepatitis C virus (HCV) is a single-strand RNA virus¹ which was previously called non-A non-B (NANB) hepatitis until the specific identification of HCV was reported in 1989.² HCV is characterized by the potential for reinfection with subtypes of the virus, and the absence of clearly defined immunity following infection.¹ It is now recognized that HCV accounted for 60-90% of what was formerly known as NANB hepatitis.³

Currently, about 150,000 new hepatitis C virus (HCV) infections occur in the United States annually. It is estimated that 1.5% or nearly 2,200 of these cases are occupationally acquired.⁵ The population prevalence of HCV is unknown since most studies have examined select populations rather than a sample of the general population. However, HCV prevalence appears low since a rate of .6% was found among blood donors in the U.S.¹

Individuals at increased risk for HCV include hemophiliacs, intravenous drug users, recipients of transfusions and organ transplants, and individuals undergoing hemodialysis.⁶⁻⁹ Sexual transmission among heterosexuals and homosexuals may occur¹⁰; evidence for sexual transmission weakens, however, when other risk factors are controlled.¹ The rate of perinatal transmission in infants born to anti-HCV-positive mothers varies from 0-13%. High titers of HCV RNA in mothers appear to favor transmission.¹¹ Other household con-

tact studies have shown HCV infection rates of 0-20% among children living with chronic HCV patients.¹¹ HCV has also been transmitted by human bites.^{12,13}

Clinical Presentation and Diagnosis

Following an average incubation period of 50 days (range 15-150 days), a patient presenting with HCV may experience general malaise and weakness followed by anorexia, nausea, vomiting, and dull right upper quadrant pain.¹⁴ However, there is considerable variation in the clinical manifestations of HCV, and there are no specific symptoms distinguishing one type of hepatitis from another.⁵

The mortality rate for all HCV infections is 5-7%.¹ Of the 150,000 individuals infected each year, it is estimated that only 37,500 become symptomatic; however, 93,000 may ultimately develop chronic liver disease and 30,700 more may develop cirrhosis.¹ It is estimated that from 50%-90% of HCV infections will lead to chronic infections and intermittent viremia, which in turn can lead to cirrhosis or hepatocellular carcinoma after a clinical latency period of two decades or more.¹

Recombinant alpha-interferon has been shown, at least in some cases, to be effective in treating chronic HCV, by reducing aminotransferase abnormalities, and by decreasing both inflammation and the level of HCV viremia. More than half of patients responding to this treatment, how-

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ever, have a relapse after completion of therapy.¹ In addition, adverse reactions and the lack of data on whether interferon will reduce the risk of developing cirrhosis or liver cancer complicate treatment.

Diagnostic Tests

Following the identification of HCV, tests quickly became available to diagnose HCV infection. In 1989 the development of the first-generation enzyme-linked immunosorbent assay (ELISA-1) for HCV was announced.¹⁵ The ELISA-1 tests serum for the presence of IgG antibody against the c100-3 antigen, and allows for detection of antibodies within about 15 weeks of infection. There is a seronegative window phase, during which infected patients have negative test results. The first-generation HCV assay was found to be 80-90% sensitive (detected 80-90% of those who were positive), but was associated with false-positive results.^{1,16} Consequently, second-generation tests were sought to overcome these shortcomings.

Second-generation assays, ELISA-2, with additional recombinant antigens from the viral genome, became available in 1992.¹⁷ Whereas the first-generation anti-HCV assays detect antibody to the c100-3 antigen, the second-generation assays combine c100-3 with another nonstructural protein, c33c, to form a new antigen known as c200. The second-generation assays also detect antibody to c22-3 antigen in the viral core.¹⁷

The second-generation tests have higher sensitivity and allow for earlier diagnosis because the antigens that are tested for are usually detectable before antibodies to c100-3 appear.¹ The second-generation tests are up to 98% sensitive, improving sensitivity over the first-generation test by about 20%.¹⁷ To further improve sensitivity and

specificity, third-generation assays have been developed, but they have not yet been approved for commercial use in the U.S.^{18,19} Recombinant immunoblot assay (RIBA) is also available and is often used as a supplementary confirmatory test to limit false-positive results. Reverse transcription/polymerase chain reaction (RT-PCR) is used to detect HCV RNA, and the results of this assay may have a bearing on management of patients. Because of its low reliability, results of HCV PCR should be interpreted with caution.²⁰

Prevalence of HCV in Health Care Workers

In the United States, the overall prevalence of HCV in health care workers is 1.4%-1.6%, a rate similar to that seen in volunteer blood donors.^{1,21-23} By comparison, 3%-35% of health care workers studied in the 1970s had antibodies to HBV; and subsequent studies of the seroprevalence of HIV demonstrated that .4% of health care workers at risk for blood exposures were HIV positive.¹ It is hypothesized that the difference in occupational risk between HBV and HCV is due to the fact that HBV circulates in higher titers, rendering the risk of HBV transmission following a needlestick between 6% and 30%.^{24,25}

In a U.S. study⁴ in which retrospective testing of serum samples drawn in 1983 from 1,677 hospital employees was conducted, 1.4% of the employees had antibodies to HCV. In this study, factors significantly associated with the presence of HCV antibody included antibody to HBV core antigen, a history of blood transfusion, and needlestick injuries. Maintenance staff and food service employees had significantly higher rates of antibody to HCV. No relationship was found between antibody to HCV and ethnic group. In addition, there was no association between antibody to HCV and years

in the same occupation or in the same hospital work area.

A British study reported a lower rate (.28%) than the U.S. study of HCV-positive health care workers among those at risk for exposures to bloodborne pathogens.²⁶ In Italy, on the other hand, an HCV prevalence rate of .85% was found among 937 health care workers, leading the authors to conclude that hospital personnel appear to be at no greater risk for HCV infection than the general population.²⁷ These researchers observed no significant difference between the HCV prevalence rate in HBV-positive versus HBV-negative health care workers.

Another Italian study compared the rate of HCV in health care workers to factory workers and found no significant difference in the prevalence of infection, suggesting the risk factors for HCV are primarily socioeconomic.²⁸ More recently, two Italian studies which did not account for sexual or other behavioral risk factors such as IV drug use found 2% and 2.2% prevalence rates of HCV among health care workers tested in 1985 and 1992, respectively.^{29,30} In these studies, history of blood transfusion was the only risk factor significantly associated with HCV infection. In general, European studies have concluded that the prevalence of HCV in health care workers is between 1%-4%.^{23-26,31-34}

In an Indian study of 50 pathology department personnel, 17 anesthesiologists, 11 cardiologists, nine gastroenterologists and three internists, no HCV antibodies were reported.³⁵

A Japanese report found the prevalence rate of HCV infection to be 4.3% (5/115) in medical staff, 2.2% (15/670) in nurses and 5.5% (10/183) in acupuncturists. The prevalence of HCV infection among those with direct patient contact was slightly, but not significantly, higher.³⁶

When subsets of health care

workers with increased risk of exposure to blood are studied, the prevalence of HCV-positive health care workers is higher. A Belgian study reported an HCV prevalence rate of 4.1% in hemodialysis nurses.³⁷ The authors ruled out non-occupational variables as risk factors for the high prevalence of HCV and suggested that the high rate may have been associated with the long duration of employment.

There are conflicting reports about the risk of HCV infection among dentists and oral surgeons. In one study, dentists and oral surgeons were found to be at increased risk, with HCV antibody found in 1.7% (8/456) dentists compared to .13% (1/723) controls. Oral surgeons were at even greater risk than other dentists, with HCV antibodies found in 9.3% (4/43) oral surgeons compared with .97% (4/413) dentists.³⁸ In contrast, a study conducted in Taiwan found that there was no increased risk of HCV infection in dentists, with a positivity rate of .6% (3/461) using a second-generation assay.³⁹ Likewise, a study of dental surgeons in south Wales did not show any HCV-positive samples among the 94 dental surgeons tested.⁴⁰

Risk of HCV Infection to Health Care Workers Following Needlestick Injury

There have been several cases reported in the literature of HCV transmissions following needlestick injuries to health care workers. Prior to the development of diagnostic tests for HCV, there was a report of transmission of NANB hepatitis via a needlestick in a medical student who suffered a deep puncture wound of a finger with a contaminated needle. The source patient had a history of kidney transplant and multiple transfusions, and was undergoing immunosuppressive therapy.⁴¹

By 1990, the first case of HCV

transmission following a needlestick injury was reported in a surgeon who was stuck by a needle from a patient known to be an HIV-positive IV drug user.⁴² Another 1990 report from West Germany described HCV transmission to a nurse who sustained a deep puncture wound to her finger from a contaminated needle. The source patient was on hemodialysis and the injury occurred two weeks after the patient experienced an increase in serum alanine aminotransferase levels.⁴³

Another report involved an incident in 1972 of HCV transmission via a needlestick injury to a nurse's finger while she was removing a hypodermic needle from a patient's arm. Sera were stored from the date of the needlestick and from six weeks following the needlestick. Serum drawn immediately after the injury was negative, but the serum drawn six weeks after the injury was positive for anti-HCV. The nurse remains positive today.⁴⁴

A report from a Spanish institution found evidence of HCV seroconversion in a physician who punctured his finger with biopsy forceps that were contaminated with extracellular fluid and blood.⁴⁵

Another reported case demonstrates the need for a test which can directly detect infectious HCV particles, both for screening blood donors and for the early diagnosis of HCV infection.⁴⁶ In this case, a nurse was injured by a contaminated needle used on a hemodialysis patient who had received a unit of packed red cells from a volunteer blood donor. First- and second-generation assays were performed on the patient's and the nurse's blood; both were negative for HCV antibodies at the time of exposure. However, 17 weeks after the transfusion, the patient's ALT concentration rose, and HCV RNA was detectable at 23 weeks. The findings remained negative for anti-HCV using first- and

second-generation assays until more than 32 weeks after transfusion. The nurse became symptomatic 13 weeks after the needlestick, and serum HCV RNA was detectable. But she remained negative for anti-HCV until she seroconverted three weeks later. Retrospective study of the blood donor showed no indication of HCV infection by commercially available ELISA tests, but HCV sequences were detectable by polymerase chain reaction.

In addition to anecdotal reports of HCV seroconversions following needlesticks, there have been several studies of the risk of HCV transmission following such injuries. An Italian study, which included nine dialysis centers, found a 39.4% prevalence of HCV among patients. The investigators followed 61 health care workers who sustained needlestick injuries, 29 who experienced mucous membrane contaminations, and 40 who had non-intact skin contacts with blood from HCV-positive patients. None of the HCV-exposed health care workers seroconverted to HCV during a ten-month follow-up period.⁴⁷ A subsequent Italian study looked at 646 HCV-exposed health care workers who were seronegative for HCV at the date of exposure and who were followed for six months; this study documented four (1.2%) HCV seroconversions, including two surgeons and one nurse who sustained needlestick injuries from blood-drawing needles, and a nurse injured by a needle used for intramuscular injection.⁴⁸

Another Italian study evaluated the risk of HCV infection following 225 exposures to HCV-positive blood in hospital personnel. Three (1.3%) cases of HCV seroconversion⁴⁹ occurred following needlestick injuries. The first, in a surgeon, involved a needle from a patient with a history of transfusions who was anti-HCV positive. The

second, also in a surgeon, was caused by a needle from an HIV- and HBV-positive intravenous drug user. The third case involved a sanitation worker who was stuck by a needle inappropriately discarded in a trash bag.

Early Japanese studies using first-generation tests for HCV found a 4% transmission rate for HCV following a needlestick injury where the source patient was anti-HCV positive.⁵⁰ Subsequent studies conducted in Japan and the U.S. using the more sensitive second-generation tests found the risk of HCV transmission following a needlestick injury to be 6-10%.^{4,51} In the U.S. study, 1,387 source patients (12.7%) were anti-HCV positive⁵, and a 6% HCV transmission rate was found. However, these data were not collected prospectively on a single cohort, but were based on sera samples that had been stored for up to 10 years. This compares to a median rate of 1.6% across studies of HCV needlestick transmission.⁴⁸

The incidence of clinical NANB hepatitis among health care workers in the U.S. study⁵ was three times higher than that of the general population. However, direct comparison of the U.S. data with population data should be undertaken with caution because NANB hepatitis is the most underreported of all types of hepatitis, and the incidence of NANB hepatitis varies widely among and within geographical areas.⁴⁸ On the other hand, Italian authors have followed up serologically 2,622 health care workers for one year and have observed three seroconversions (0.1%) in subjects who did not acknowledge occupational or community risk factors.³⁰ They found that source patients with renal or liver disease, HIV infection, or with a history of IV drug use were more likely to have HCV infection than other patients, and that the highest rate of reported exposure to HCV occurred

in the emergency department.

The difference in rates reported in these studies likely reflects differences in study designs, diagnostic methods, exposure mechanism (hollow-bore vs. solid needles), number of cases followed, and different infectivity of HCV strains.⁵²

Consequently, the risk of HCV transmission from a single needlestick injury appears to be lower than the 7-30% risk of contracting HBV.⁵³ Using a deterministic model that takes into account the anti-HCV seroprevalence among dialysis patients, the rate of occupational exposures among dialysis health care workers, and the probability of HCV transmission, the risk of acquisition of HCV among dialysis health care workers has been calculated as 0.06 and 0.0087 per 10,000 dialysis procedures performed for percutaneous injuries and mucous membrane contaminations, respectively.⁵⁴

Consequences and Prevention of HCV Infection

Currently there is no vaccine available for HCV. Because HCV is characterized by genetic and serological heterogeneity, by the absence of a clearly defined protective immune response after infection, and by the possibility of reinfection, the development of a vaccine is difficult.^{1,55} There has been some success reported in a study in which chimpanzees were protected following immunization with recombinant DNA derived from HCV.¹ However, it will likely be several years before a vaccine is available. Furthermore, it has not been determined whether the administration of immune serum globulin provides protection against parenteral exposure to HCV.¹

The studies cited above demonstrate the need for prospective, comprehensive surveillance in which follow-up serologies are reported for HIV, HCV and HBV so that valid

comparisons may be made regarding the incidence, prevalence, and mechanisms of transmission for each virus. In addition, research indicates that parenteral exposure to HCV via needlestick injuries represents a significant transmission risk for health care workers. This underscores the need for protective devices which reduce needlestick risk; in addition, good disposal systems which provide puncture-resistant containers close to the point of use should be routinely used.

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