Risk and Prevention of Hepatitis C Virus Infection

Implications for Dentistry

A B S T R A C T

Background. The occupational risk of hepatitis C virus, or HCV, infection in dentistry is very low. Nonetheless, the lack of an effective vaccine, the high rates of chronic infection and the limited effectiveness of treatment may cause concern for dental workers who come into contact with blood in their daily practices.

Description of the Disorder. The authors discuss the natural history, diagnosis and treatment, and patterns of transmission of HCV infection, including the Centers for Disease Control and Prevention's recommendations for management and follow-up of health care workers after occupational exposure to HCV.

Clinical Implications. In the absence of an effective vaccine or postexposure prophylaxis, prevention of occupational transmission of HCV in dental settings continues to rely on the use of universal precautions, including barrier precautions and the safe handling of sharp instruments.

During the past two decades, published reports have alerted dentists and other dental workers to the potential risk of infection with bloodborne pathogens while providing patient care. For example, studies conducted before hepatitis B vaccine became available in 1982 indicated that dentists and oral surgeons had a higher prevalence of hepatitis B virus, or HBV, infection than most other health care workers, or HCWs, and a severalfold higher prevalence than the general population.[1-3]

In 1981, the first cases of AIDS were recognized, and in 1988, possible occupational transmission of the human immunodeficiency virus, or HIV, to a dentist with no reported behavioral or transfusion risks for HIV was reported.[4] In the late 1980s, hepatitis C virus, or HCV, the cause of most cases of non-A, non-B hepatitis in the United States, was discovered. Although the risk of HCV infection among HCWs is lower than that for HBV infection, some evidence exists of occupational transmission of HCV. In this report, we discuss general characteristics, risk and prevention of HCV infection, including the Centers for Disease Control and Prevention's, or CDC's, recommendations for follow-up of HCWs after occupational exposure to HCV.

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BURDEN OF DISEASE

H CV is an RNA virus that proliferates in the liver and circulates in the blood of infected people. HCV is a major cause of chronic liver disease in the United States and worldwide and is the primary reason for liver transplantation in the United States. An estimated 3.9 million Americans (1.8 percent) are infected with HCV, according to the findings of the Third National Health and Nutrition Examination Survey, conducted from 1988 through 1994.[5] The majority of these people are chronically infected, yet may not be aware of their infection because they remain asymptomatic.

People with chronic HCV infection are potentially infectious to others and are at risk of developing chronic liver disease, including cirrhosis and hepatocellular carcinoma. An estimated 8,000 to 10,000 deaths result each year from chronic liver disease associated with HCV infection, although deaths from fulminant acute hepatitis C are rare.[6] Health care costs related to acute and chronic hepatitis C are considerable; in 1992, the estimated total annual cost was in excess of $600 million.[6]

NATURAL HISTORY

Most people with acute HCV infection (60 to 70 percent) do not experience overt clinical illness, 20 to 30 percent may exhibit jaundice and 10 to 20 percent may have nonspecific symptoms such as loss of appetite, fatigue and abdominal pain. The mean incubation period for acute HCV infection is six to eight weeks, with a range of two weeks to six months. However, HCV RNA can be detected in the blood as soon as one week after initial exposure. In approximately 90 percent of patients, antibodies to HCV, or anti-HCV, can be detected within three months after onset of infection (on average, within eight to 10 weeks).[7]

Despite the development of anti-HCV, the genetic diversity of HCV and its ability to mutate rapidly prevent the development of an effective neutralizing immune response, leading to a high rate of chronic infection.[8] Thus, about 85 percent of

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HCV-infected patients fail to clear the virus by six months and develop chronic (persistent) HCV infection; of these, 60 to 70 percent will develop chronic hepatitis and 10 to 20 percent will eventually develop more serious long-term sequelae, such as cirrhosis and liver cancer.[9]

Distinguishing acute HCV infection from chronic HCV infection can be difficult. In general, people with chronic infection will display persistently elevated serum alanine aminotransferase, or ALT, levels more than six months after acute infection. In patients with chronic HCV disease, however, ALT levels may fluctuate between periods of elevation and periods of normal or near-normal levels. Normal ALT levels, therefore, do not necessarily indicate lower viral titers or absence of infection. In fact, detectable levels of HCV RNA and pathological liver disease have been found in patients with persistently normal ALT levels.[10] Researchers have not identified any clinical or epidemiologic factors to accurately predict which acutely HCV-infected people will progress to persistent infection or chronic liver disease.[11]

Unfortunately, chronic hepatitis is often not recognized until symptoms of advanced liver disease appear, which may take as long as two or three decades. Although there are no predictors for progression to active liver disease, recent data indicate that being male, older than 40 years at infection and consuming 50 grams or more of alcohol daily are associated with more severe liver disease.[12] In some studies, disease severity also has been associated with being infected with genotype 1b.[13]

DIAGNOSIS AND TREATMENT

Tests that detect anti-HCV include the enzyme immunoassays, or EIAs, which are reproducible, inexpensive and suitable for screening low- and high-prevalence populations and for use as an initial test for patients with clinical liver disease.[14] These assays detect anti-HCV in 97 percent of infected people, but are limited because they do not distinguish among acute, chronic or resolved infec-

tion. In addition, in many populations with a low prevalence of HCV infection, including HCWs, the rate of false-positivity for anti-HCV is high.[9,15] Thus, supplemental assays, such as the recombinant immunoblot assay, or RIBA, should be used to verify a positive anti-HCV result by EIA.

Qualitative detection of HCV RNA by polymerase chain reaction, or PCR, will indicate whether a patient has viremia. However, because the detection of HCV RNA may be intermittent, a single negative test result does not confirm that the patient has recovered from HCV infection. Interpretation of PCR results also is limited because these assays are not standardized; thus, results may vary considerably among laboratories.

Researchers have evaluated several different forms of interferon in the treatment of patients with chronic HCV infection. The efficacy of treatment is measured by normalization of serum ALT levels and the loss of detectable HCV RNA in serum. Therefore, serial ALT testing and testing for HCV RNA via qualitative PCR at various intervals are recommended for monitoring biochemical and virologic responses to therapy.[14] Although injections of interferon alfa, or IFN-α, have been shown to benefit some patients,[16] only 10 to 20 percent of patients exhibit sustained response rates to IFN-α therapy, and up to 15 percent experience side effects severe enough to discontinue treatment. In addition, no indicators have been identified to predict which patients will sustain a long-term remission in response to IFN-α therapy.

Recent reports have shown that the combination of IFN-α

and ribavirin, an oral antiviral agent, can lead to a substantial increase in sustained virologic response rates (40 to 50 percent) compared with response rates for IFN-α alone (15 to 25 percent).[17-20] Patients who receive ribavirin therapy should be monitored closely for adverse side effects. The Food and Drug Administration has approved the use of combination therapy with ribavirin to treat patients

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with chronic hepatitis C who have experienced relapse after undergoing IFN-α treatment[6] and, more recently, for patients who have not been treated with IFN-α.

PATTERNS OF TRANSMISSION

The most efficient mode of HCV transmission is through percutaneous blood exposure; thus, the highest prevalence of anti-HCV (60 to 90 percent) is found among people with large or repeated direct percutaneous exposures to

blood, such as patients with hemophilia and injecting drug users, or IDUs. Researchers have found a moderate prevalence (10 to 30 percent) among recipients of blood transfusions before 1990 and among patients undergoing hemodialysis. The prevalence is lower (1 to 10 percent) among people with high-risk sexual behaviors, or sexual or household contacts with people who have chronic HCV infection, as well as among HCWs (including dental workers) and the general population (1 to 2 percent).[11] The prevalence of HCV infection is lowest among volunteer blood donors (0.3 percent).[21] However, infection rates in blood donors are not representative of rates in the general population because people with a history of hepatitis or other risk factors for blood-borne infections are asked not to donate.

Before donor populations and blood began to be screened for HCV infection, transfusion recipients accounted for a substantial proportion of cases of newly acquired HCV infections. Since 1992, when routine screening of blood and donor populations was implemented, the risk of transfusion-associated HCV infection became negligible. The majority of reported cases of acute HCV infections (> 60 percent) continue to occur among IDUs—an estimated 50 to 60 percent of IDUs become infected within six months of beginning injection drug use.[22]

Among IDUs, HCV infection is four times more common than infection with HIV. In contrast with transmission of hepatitis B virus, sexual transmission of HCV appears less efficient, accounting for only 10 to 20 percent of newly acquired infections.

TABLE

HEPATITIS C VIRUS SEROPREVALENCE IN U.S. DENTISTS.

SOURCE	STUDY PERIOD	LOCATION	DENTISTS IN THE STUDY	NO. OF DENTISTS TESTED	NO. (%) OF DENTISTS WITH POSITIVE ANTI-HCV* TEST RESULTS
Klein and colleagues[36]	1985-1987	New York City	General dentists and oral surgeons	456	8 (1.7)
Gerberding[27]	1984-1992	San Francisco	Hospital and community dentists	54	0 (0.0)
Gruninger and colleagues[37]	1989	ADA Annual Session Honolulu	General dentists	1,437	1 (< 1.0)
Wisnom and colleagues[38]	1992	Maryland	General dentists	291	2 (< 1.0)
Thomas and colleagues[39]	1992	AAOMS meeting Honolulu[†]	Oral surgeons	343	7 (2.0)
		ADA Annual Session Orlando, Fla.	General dentists	305	2 (0.7)

* HCV: Hepatitis C virus.
† AAOMS: American Association of Oral and Maxillofacial Surgeons.

Less frequently, cases have been reported to occur from exposure to household contacts who have chronic HCV infection.[6]

The CDC currently recommends routine screening for HCV infection only for people who belong to groups with a known high prevalence of HCV infection, including those who have injected illegal drugs (even once), recipients of transfusions or solid organ transplants before 1992, recipients of clotting factor concentrate manufactured before 1987, people with persistently high ALT levels and patients receiving long-term hemodialysis.[6]

OCCUPATIONAL TRANSMISSION

As stated above, HCV is most efficiently transmitted through percutaneous exposures to blood. Therefore, HCWs exposed to blood during the provision of care are at risk of acquiring HCV infection, although the risk factors for occupational transmission are not well-defined. Between 1984 and 1992, several seroprevalence studies of surgeons and hospital-based HCWs found a prevalence of HCV infection of about 1 percent.[22-27] Follow-up studies of HCWs exposed to HCV-infected blood through percutaneous or other sharp-instrument injuries found that the incidence of anti-HCV seroconversion averaged 1.8 percent (range, 0 to 7 percent).[9,28-32] In the only study that detected HCV RNA by PCR, the incidence of postexposure seroconversion was 10 percent.[32] Although these studies did not document seroconversion associated with mucous membrane or nonintact skin exposure, at least two cases of transmission of HCV from a blood splash to the conjunctiva have been reported.[33,34]

In a report from Spain, Esteban and colleagues[35] found that five patients who underwent open-heart surgery and who had documented acute HCV infection appeared to have acquired their infection from a cardiac surgeon with chronic hepatitis C. Although the precise mode of transmission was not identified, available evidence suggests that transmission was associated with percutaneous injuries, most of which were caused by wires during closure of the sternum.

Few data exist to estimate the occupational risk of HCV infection in dentistry. However, most studies suggest that the prevalence of HCV infection among dentists, surgeons and hospital-based HCWs is similar to that among the general population (1 to 2 percent) (Table).[27,36-39] Using blood samples collected in the New York City area from 1985 to 1987, Klein and colleagues[36] found that the prevalence of anti-HCV was higher among dentists (1.7

percent) than among blood donors (0.14 percent). However, for reasons stated above, blood donors may not be an appropriate comparison group. A small sample of these dentists (n = 43) who performed primarily oral surgical procedures had an anti-HCV prevalence of 9.0 percent.

From 1984 to 1992, a prospective study of hospital-based dental workers in San Francisco found that none of the 54 dental workers who were followed up during the eight-year study period experienced HCV antibody seroconversion.[27] Similarly, less than 1 percent of dental HCWs in the Baltimore area tested positive for anti-HCV in 1992.[38] Another study, conducted from 1991 to 1992 in North America, found anti-HCV seroprevalence rates of 2.0 percent and 0.7 percent among oral surgeons and dentists, respectively.[39] In this study, anti-HCV was more prevalent among dentists who were older, had more years in practice and had serologic evidence of previous HBV infection. It is not surprising to find an association between anti-HCV and past HBV infection, because both viruses are transmitted via the blood-borne route.

Because of differences in study sites, sample sizes, types of HCWs and assay methods, it is difficult to interpret the results of these studies. For example, although Thomas and colleagues[39] found an association between HBV infection and anti-HCV, this association was not found among New York City dentists[36] or orthopedic surgeons.[26] Furthermore, in one study that assessed risk factors for HCV infection among hospital employees, a history of accidental needle sticks was independently associated with

anti-HCV positivity.[25] In contrast, studies of orthopedic or hospital-based surgeons, general dentists and oral surgeons failed to find a correlation between a history of percutaneous injury in the previous month and HCV infection.[24,36,39] In summary, although these studies indicate a possible occupational

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risk of HCV infection, this risk appears to be relatively low. More data are needed to determine the magnitude of the risk and specific factors that may affect the likelihood of HCV transmissions in health care settings, including dentistry.

PREVENTING OCCUPATIONAL TRANSMISSION

The virus' ability to escape the immune system has created difficulties in the development of an effective vaccine. This characteristic also may explain why immune globulin, or IG, is not effective in preventing hepatitis C. Preventing acute HCV infection through postexposure use of antiviral agents, such as IFN-α, has not been thoroughly evaluated, and an established infection may need to be present for IFN-α to be an effective treatment.[40] On the basis of these considerations, CDC does not recommend IG or antiviral agents for postexposure prophylaxis of hepatitis C.[41]

Therefore, prevention of occupational transmission of HCV in health care settings, including dentistry, continues to rely on the use of universal precautions, including the appropriate use of barrier precautions (for example, gloves, masks and protective eyewear) and the safe handling of sharp instruments to prevent occupational exposures to blood.[42] Strategies for dental professionals to prevent injuries from sharp instruments include safe work practices (for example, using an instrument instead of fingers to retract tissue), safer instrumentation or design (for example, self-sheathing needles, changes in dental unit design) and continued education of HCWs.[43]

Even in the absence of effective postexposure prophylaxis, HCWs with an occupational exposure to HCV may benefit from knowing their infective status, so they can seek ongoing evaluation for chronic liver disease and treatment. In addition, studies have found higher rates of resolved infection when IFN-α treatment was initiated early in the course of the disease.[44] We do not know, however, whether antiviral treatment

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is more effective when begun in the acute phase of infection or during the early course of chronic HCV infection.

Current CDC guidelines recommend that individual health care institutions consider implementing policies and procedures for follow-up after percutaneous or permucosal exposures to blood.[41] At a minimum, such policies should include the following measures:

▪ for the source person, baseline testing for anti-HCV;

▪ for the person exposed to an anti-HCV–positive source, baseline and follow-up testing (for example, at six months) for anti-HCV and liver enzyme activity;

▪ confirmation by supplemental anti-HCV testing (for example, RIBA) of all anti-HCV results reported to be repeatedly reactive by EIA;

▪ avoidance of postexposure prophylaxis with IG or antiviral agents;

▪ education for HCWs about the risk and prevention of blood-borne infections, including hepatitis C, in occupational settings, with information routinely updated to ensure accuracy.

Currently, no recommenda-tions exist regarding practice restrictions for HCWs with hepatitis C.[6] The risk of transmission from an infected HCW to a patient appears to be very low. Furthermore, no serologic assays can determine infectivity and no data exist to determine the threshold concentration of virus required for transmission. As recommended for all HCWs, those who have tested positive for anti-HCV should follow strict aseptic techniques and universal precautions, including appropriate use of hand washing and protective barriers as well as care in the use and disposal of needles and other sharp instruments.

SUMMARY

Almost 4 million Americans are chronically infected with HCV, four times the estimated number of HIV infections. Because of the insidious nature of this disease, many people remain unaware of their HCV infection until symptoms of serious liver damage appear. Current CDC recommendations include counseling and testing of people at risk of acquiring HCV infection so that, if infected, they may benefit from medical evaluation and treatment.

On the basis of evidence from seroprevalence studies among various types of HCWs, including dental workers, we can conclude that the risk of occupationally acquired hepatitis C appears to be very low. Nonetheless, the lack of an effective vaccine, the high rates of chronic infection and the limited efficacy of treatment for HCV infection are cause for concern by dental workers who contact blood in their daily practices. Strict adherence to the use of universal precautions and continued education of dental workers about the risk and prevention of blood-borne infections remain the most effective prevention strategy. ▪

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For further information on hepatitis, contact CDC's toll-free number (1-888-4HEP-CDC) or visit the Hepatitis Branch Web site at "http://www.cdc.gov/ncidid/diseases/hepatitis/".

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