Prevention of Spread of Hepatitis C

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Hepatitis C virus (HCV) is transmitted by percutaneous or permucosal exposure to infectious blood or blood-derived body fluids. Based on the results of cohort and acute case control studies, risk factors associated with acquiring HCV infection in the United States have included transfusion of blood and blood products and transplantation of solid organs from infected donors, injecting drug use, occupational exposure to blood (primarily contaminated needle sticks), birth to an infected mother, sex with an infected partner, and multiple heterosexual partners. Nosocomial and iatrogenic transmission of HCV primarily are recognized in the context of outbreaks, and primarily have resulted from unsafe injection practices. Transmission from HCV-infected health care workers to patients is rare. Transfusions and transplants have been virtually eliminated as sources for transmission, and most (68%) newly acquired cases of hepatitis C are related to injecting drug use. The primary prevention of illegal drug injecting will eliminate the greatest risk factor for HCV infection in the United States. Other prevention strategies that need to be widely implemented include risk reduction counseling and services and review and improvement of infection control practices in all types of health care settings. Testing for HCV infection should be routinely performed for persons at high risk for infection or who require postexposure management. There are no recommendations for routine restriction of professional activities for HCV-infected health care workers, and persons should not be excluded from work, school, play, and child care or other settings on the basis of their HCV infection status. (HEPATOLOGY 2002; 36:S93-S98.)

To prevent the spread of hepatitis C virus (HCV), prevention and counseling measures should be appropriate to the presence and magnitude of risk. Assessing risk is based on the epidemiologic characteristics of HCV, including modes of transmission, which persons are at increased risk or have a high prevalence of infection, and the amount of disease or infection attributable to the risk. In 1998, the Centers for Disease Control and Prevention (CDC) convened a meeting of expert consultants to review the available data and develop recommendations for the prevention and control of HCV infection. These recommendations were published in October 1998.[1] This review summarizes highlights of the epidemiologic data used to support these recommendations and includes data that have become available since that publication.

Risk Factors Associated With Acquiring HCV Infection

The most reliable data on risk factors associated with acquiring infection are obtained from cohort (prospective) studies and case control (retrospective) studies of acute disease.[2] In cohort studies of HCV infection, the presence of exposure (*e.g.*, blood transfusion) was determined in a defined population (*e.g.*, hospitalized patients), and the population was followed to compare the incidence of infection and disease in the exposed group compared with the incidence in the nonexposed group. In case control studies of acute hepatitis C, the population sample was selected based on the presence or absence of newly acquired, symptomatic disease, and the proportions of cases with histories of various exposures (*e.g.*, blood transfusion, injection drug use, number of sex partners) during the 6 months before onset of disease were compared with those of the controls. For these studies, cases were identified from among persons seeking medical care for acute viral hepatitis in public and private outpatient and inpatient settings and the controls were selected

Abbreviations: HCV, hepatitis C virus; CDC, Centers for Disease Control and Prevention; HBV, hepatitis B virus; STD, sexually transmitted disease; anti-HCV, antibody to hepatitis C virus.

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to be representative of the populations from which the cases were drawn.

Risk factors identified by these studies in the United States included transfusion of blood and blood products and transplantation of solid organs from infected donors, injecting drug use, occupational exposure to blood (primarily contaminated needle sticks), birth to an infected mother, sex with an infected partner, and multiple heterosexual partners.[3-10] Potential exposures that were evaluated in case control studies of acute disease and found not be associated with acquiring hepatitis C included medical, surgical, or dental procedures, tattooing, acupuncture, ear piercing, incarceration, military service, or foreign travel.[7,8] While recent histories of health care-related procedures were commonly reported by both cases and controls (about 30%), a recent history of potential exposures such as tattooing was reported by less than 1% of both cases and controls. Ongoing surveillance for cases of acute hepatitis C indicate that this proportion has not increased over time (CDC, unpublished data).[1]

One of the major limitations of cohort and case control studies is their inability to detect associations with low-frequency events,[2] although such events can result in transmission. For example, health care-related procedures were not associated with acquiring hepatitis C when evaluated in case control studies. However, outbreaks of HCV infection have been recognized in chronic hemodialysis, hospital inpatient, and private practice settings (CDC, unpublished data).[11] These outbreaks were associated with use of contaminated equipment and unsafe injection practices, including reuse of disposable needles and syringes and contamination of multiple-dose medication vials. Similarly, prospective studies of health care workers after occupational exposures have identified transmission only after contaminated needle sticks[1,9]; although there have been case reports of HCV transmission from blood splashes to the eye.[12,13]

Even more rarely, HCV-infected health care workers have transmitted to patients. There have been 8 documented episodes reported worldwide, 2 of which occurred in the United States.[14-19] Of those for which the mode of transmission was reported, none were associated with the performance of exposure-prone invasive procedures[14,15,17-19]; rather, most were the result of contamination of the patients' narcotics used by the health care worker for self-injection, including the 2 reported episodes in the United States.[18,19] In addition, unlike the risk for transmission of hepatitis B virus (HBV) from an infected health care worker, the risk for transmission of HCV was extremely low (averaging about 0.5%), even for those episodes involving surgeons. Furthermore, 2 retrospective investigations of HCV-infected surgeons found no evidence for transmission to their patients (CDC, unpublished data).[20]

Thus, health care-related HCV transmissions are relatively rare events; therefore, studies of sporadic or background infections cannot demonstrate an epidemiologic association with such exposures. Among those episodes that have been recognized, patient-to-patient transmission has primarily been because of unsafe injection practices. Of the episodes linked to infected health care workers, at least two thirds were not related to exposure-prone invasive procedures, and half were related to the infected health care worker's substance abuse.

Cross-sectional or prevalence studies also have evaluated a variety of known and potential risk factors for transmission. In these studies, both the potential exposure and the disease outcome were determined simultaneously. Study populations included volunteer blood donors[21,22]; highly selected patient groups identified in a gastroenterology clinic,[23] an orthopedic spinal clinic,[24] a veterans affairs hospital,[25] and a sexually transmitted diseases (STD) clinic (CDC, unpublished data); unselected groups of college and university students; and a group of juvenile detainees (CDC, unpublished data). All of these studies identified injection drug use, and most identified blood transfusion from unscreened donors, as associated with HCV infection. In contrast, a history of intranasal cocaine use was identified as a possible risk factor in only 1[21] of 6 studies in which it was evaluated, although about 10% of the populations studied admitted to a history of this behavior. In addition, this behavior rarely has been reported by cases with acute hepatitis C who denied injection drug use (CDC, unpublished data).[1]

Tattooing was identified as a possible risk factor in 3 of the studies of selected patient groups,[23-25] but not in the other 5 studies in which it was evaluated. In 2 of the studies of clinic patients, the attributable fractions (i.e., the proportion of HCV infections estimated to be attributable to tattooing) were widely divergent and ranged from less than 1% among the gastroenterology clinic patients[23] to 40% among the orthopedic spinal clinic patients.[24] There also was considerable inconsistency between studies that evaluated body piercing, and most did not distinguish ear piercing from piercing of other body parts. In 1 study of volunteer blood donors, only ear piercing among men was identified.[21] In 2 studies in which body piercing other than ears was reported by 20% or more of the participants, there was no positive association (CDC, unpublished data). None of the studies identified acupuncture as a potential risk factor for hepatitis C.

Cross-sectional or prevalence studies can identify possible associations requiring further study; however, be-

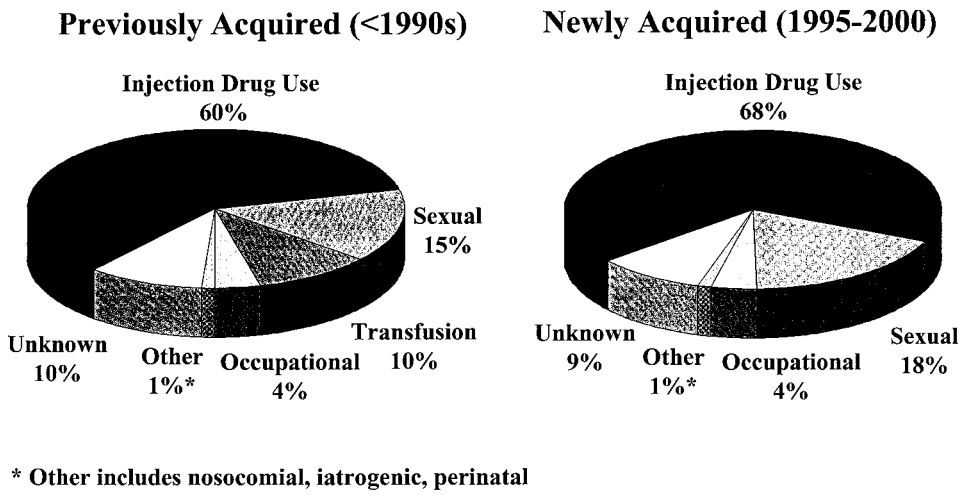

Fig. 1. Sources of infection for hepatitis C. (Data from the Centers for Disease Control and Prevention, Atlanta, GA.)

cause the temporal relationship between exposure and infection usually is unknown, the results of these studies cannot establish associations or causal relationships.[2] Furthermore, results from highly selected groups may not be generalizable to other populations, substantial differences in methodology lead to inconsistent results among studies, and results not replicated consistently cannot be interpreted as associated with infection. Although the potential exposures evaluated by these studies plausibly could result in transmission of HCV, the frequency of such transmission might be too low to detect, and there is no consistent data indicating that they are risk factors for acquiring HCV infection in the United States.

Thus, most HCV infections in the United States can be accounted for by risk factors identified by cohort studies and case control studies of acute disease; these risk factors all are associated with percutaneous or mucosal exposures to blood or blood-derived body fluids. Currently, most newly acquired cases of hepatitis C (68%) are associated with injection drug use, 18% occur among persons with no other risk factor except exposure to an infected sex partner or to multiple sex partners, 4% occur in health care workers frequently exposed to blood, and all together, nosocomial, iatrogenic, and perinatal exposures account for about 1% (Fig. 1). In only 9% of cases is a source not identified. The major difference between recently acquired cases of hepatitis C and those acquired before the 1990s is the relative contribution of blood transfusion, a source that now is extremely rare.

Persons at Increased Risk for HCV Infection

Identification of persons with chronic HCV infection is a major focus of prevention programs.[1] Testing should be routinely offered to persons most likely to be infected with HCV who might require medical management, and testing should be accompanied by appropriate counseling and medical follow-up. In addition, anyone who wishes to know or is concerned regarding their HCV infection status should be provided the opportunity for counseling, testing, and appropriate follow-up. The determination of which persons at risk to recommend for routine testing is based on various considerations, including a known epidemiologic relationship between a risk factor and acquiring HCV infection, the prevalence of the risk behavior or characteristic in the population, the prevalence of infection among those with a risk behavior or characteristic, and the need for persons with a recognized exposure to be evaluated for infection.

The presence of a risk factor is not necessarily equivalent to "increased risk." For example, histories of injecting drug use, multiple sex partners, or occupational exposures to blood all are risk factors for HCV infection. However, the prevalence of HCV infection among injecting drug users is high (60% to 90%), whereas the prevalence among STD clients is relatively low (5% overall and 2% among those who reported never injecting illegal drugs), as are the prevalences among surgeons, nurses, and emergency responders (1% to 3%).[1,26] Similarly, the prevalences among persons who have histories of snorting cocaine, tattooing, or body piercing are also low (less than 1% among those who reported never injecting illegal drugs) (CDC, unpublished data). In the general population, the prevalence of HCV infection among adults 20 to 49 years old is 4.1% for males and 1.6% for females.[27]

Based on risk factors associated with HCV infection in epidemiologic studies and a high prevalence of infection among those with these risk factors, HCV testing is routinely recommended for persons who have injected illegal drugs, received plasma-derived products known to trans-

mit HCV infection that were not treated to inactivate viruses (manufactured before 1987), received blood transfusions or solid organ transplants before July 1992, were ever on chronic hemodialysis, or have evidence of liver disease (*e.g.*, persistently abnormal levels of alanine aminotransferase).[1] Based on the need for postexposure management, HCV testing also is routinely recommended for health care, emergency medical, and public safety workers after needle stick or mucosal exposures to HCV-positive blood and for children born to HCV-positive women.[1]

Postexposure Management

Individual institutions should establish policies and procedures for HCV testing of persons after percutaneous or permucosal exposures to blood, and should ensure that all personnel are familiar with these policies and procedures. Health care professionals who provide care to persons exposed to HCV in the occupational setting should be knowledgeable regarding the risk for HCV infection and appropriate counseling, testing, and medical follow-up.

Immune globulin and antiviral agents are not recommended for postexposure prophylaxis of hepatitis C.[1] When a needle stick, sharps, or mucosal exposure to blood occurs, the source of the exposure should be tested for antibody to HCV (anti-HCV), and all repeatedly reactive results by enzyme immunoassay should be confirmed by recombinant immunoblot testing for anti-HCV.[1] There are insufficient data to determine the need for follow-up based solely on the results of testing for HCV RNA. If the source is anti-HCV positive, the exposed person should be tested for anti-HCV and alanine aminotransferase level at baseline and follow-up (*e.g.*, at 4 to 6 months). For earlier diagnosis of HCV infection, testing for HCV RNA may be performed at 4 to 6 weeks. There are no recommendations for restriction of activities during the postexposure follow-up period.

Limited data indicate that antiviral therapy might be beneficial when started early during the course of acute hepatitis C, but no guidelines exist for administration of therapy during the acute phase of infection. When HCV infection is identified early, the individual should be referred for medical management to a specialist knowledgeable in this area.[1]

Because of their recognized exposure, children born to HCV-positive women also should be tested for HCV infection.[1] Immune globulin and antiviral agents are not recommended for postexposure prophylaxis of infants born to HCV-positive women. Testing of infants for anti-HCV should be performed no sooner than 15 to 18 months of age, when passively transferred maternal anti-HCV declines below detectable levels. For earlier diagnosis of HCV infection, testing for HCV RNA may be performed at or after the infant's first well child visit at age 1 to 2 months and should be repeated. Umbilical cord blood should not be used for the diagnosis of perinatal HCV infection because cord blood can be contaminated by maternal blood. If positive for either anti-HCV or HCV RNA, children should be evaluated for the presence or development of liver disease, and those children with persistently abnormal alanine aminotransferase levels should be referred to a specialist for medical management.

Recommendations for HCV-Positive Persons

All HCV-positive persons should be referred for medical evaluation and management. They should receive hepatitis A vaccine, and if they are at risk for HBV infection, hepatitis B vaccine.[1] No restrictions are routinely recommended for HCV-positive health care workers when there is no evidence of transmission.[1] As recommended for all health care workers, those who are HCV-positive should follow strict aseptic technique and standard precautions, including appropriate use of hand washing, protective barriers, and care in the use and disposal of needles and other sharp instruments. If transmission from an infected health care worker to patients is suspected, local and state health departments should be notified and an investigation conducted to determine if such transmission occurred, the extent to which it occurred, and the factors associated with transmission. The individual circumstances surrounding such events will determine the need for and extent of any limitations or restrictions placed on the infected health care worker's practice.

Hepatitis C virus-positive persons should be advised to not donate blood, body organs, other tissue, or semen. They also should not share toothbrushes, razors, or other personal care articles that might have blood on them.

Hepatitis C virus-positive persons with a long-term steady partner do not need to change their sexual practices; however, they should discuss with their partner the need for counseling and testing, and the couple should be informed of available data on risk for sexual transmission of HCV to assist them in making decisions about precautions, including the low, but not absent, risk for transmission.[1] Hepatitis C virus-positive persons do not need to avoid pregnancy or breastfeeding, and determining the need for cesarean delivery versus vaginal delivery should not be made on the basis of HCV infection status.[1]

Hepatitis C virus is not spread by kissing, hugging, sneezing, coughing, food or water, sharing eating utensils or drinking glasses, or casual contact. Hepatitis C virus-positive persons should not be excluded from work,

school, play, child-care, or other settings on the basis of their HCV infection status.[1]

Future Needs for Prevention of HCV Transmission

Strategies for reducing or eliminating the potential risk for HCV transmission from infected donors, including screening and testing of donors and virus inactivation of plasma-derived products, have been extremely successful. However, strategies for reducing or eliminating the potential risk for HCV transmission from high-risk behaviors, such as risk reduction counseling and services, need to be more widely implemented.[1]

Health care professionals in all patient care settings should routinely obtain a history that inquires about use of illegal drugs and evidence of high-risk sexual practices, such as multiple sex partners or history of STDs. Primary prevention of illegal drug injecting will eliminate the greatest risk factor for HCV infection in the United States. Although consistent data are lacking regarding the extent to which sexual activity contributes to HCV transmission, persons having multiple sex partners are at risk of STDs such as human immunodeficiency virus, HBV, syphilis, gonorrhea, and chlamydia. Persons who inject drugs or who are at risk for STDs should be counseled on what they can do to minimize their risk of becoming infected or of transmitting infection to others, including the need for vaccination against hepatitis B.

Counseling of persons with potential or existing illegal drug use or high-risk sexual practices should be conducted in the setting in which the patient is identified. If counseling services cannot be provided on site, patients should be referred to a convenient community resource, or at a minimum, provided easy-to-understand health education material. Drug treatment and STD clinics, correctional institutions, and human immunodeficiency virus counseling and testing sites should integrate hepatitis prevention activities (*e.g.*, counseling and testing for HCV and vaccination against hepatitis B) into their settings and routinely provide information concerning the prevention of HCV and HBV infection in their counseling messages. Counseling regarding safer injection practices should include the importance of not sharing any drug injection equipment. To further reduce the risk of HCV infection among injection drug users, communities should consider increasing access to sterile syringes and needles through syringe and needle exchange programs and repeal of restrictive paraphernalia laws and regulations.

Infection control practices in all types of health care settings need to be reviewed and improved to prevent nosocomial and iatrogenic transmission of HCV (and other bloodborne pathogens). Practices in chronic hemodialysis centers should be updated according to current recommendations.[11] Staff in all health care settings should review their injection practices to ensure that disposable injection equipment is not reused. To prevent contamination of multiple dose medication vials, they should be limited to a single patient or restricted to a clean centralized preparation area.

Certain aspects of the epidemiology of hepatitis C still are not clearly defined. The risk for transmitting HCV by sexual activity, particularly between steady partners, remains unknown. Specific procedures that might be modified to prevent perinatal transmission of HCV have not been consistently identified. Because HCV transmission by both sexual and perinatal routes occurs at a relatively low frequency, studies large enough to answer these questions may not be possible. Future studies might consider focusing on identification of more specific factors that determine infectivity (*e.g.*, characteristics of the virus, phase of infection) to distinguish persons most likely to transmit HCV, and improve our ability to counsel individual patients.

Identification of HCV-infected persons also needs to be improved. Also needed are better and more focused messages that successfully reach those at high risk, improved counseling and testing practices of health care professionals, and integration of viral hepatitis prevention services into high-risk settings. Finally, the information provided about hepatitis C must be consistent and based on reliable data.

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