The A, B, C, D, and E of Viral Hepatitis: Spelling Out the Risks for Healthcare Workers

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Hepatitis as an occupational hazard for healthcare workers began to be appreciated in the United States a little over 40 years ago, with the granting of the first compensation award to a blood bank employee with serum-transmitted hepatitis. At least 32 additional cases in healthcare workers were reported within the next two years, mostly, but not exclusively, as a result of the accidental inoculation of blood or serum.

It has been only in the last 15 years, however, that the major viruses causing hepatitis have been differentiated, that the main modes of transmission have been delineated, and that some effective methods of prevention have been developed. All five of the primary hepatotropic viruses, A-E, remain a threat to healthcare workers, but the nosocomial transmission risk of each virus varies considerably, depending on certain characteristics of the patient population, the job description of the healthcare worker, and the degree of compliance with effective preventive measures such as handwashing, barrier and sharps injury precautions, and vaccination.

HEPATITIS A

Numerous studies that have evaluated the risk of hepatitis A in healthcare workers both in this country and abroad have shown no excess in the prevalence of hepatitis A antibodies in healthcare workers compared with a local general population. Furthermore, a prospective community-based study of viral hepatitis incidence and risk factors also has not shown healthcare work to be a major risk factor for acquisition of hepatitis A virus. However, under certain circumstances, nosocomial transmission of hepatitis A virus to healthcare workers has been well documented to occur most often via a fecal/oral route. Other body substances such as saliva and urine do not appear to represent a hazard for hepatitis A transmission. Parenteral transmission via needlestick injury from a source patient who happens to be viremic during the asymptomatic incubation period of hepatitis A is theoretically possible but has not been reported.

Fecal/oral transmission of hepatitis A virus to healthcare workers can, on rare occasions, occur via contaminated food but almost always occurs directly from person to person. Essentially all such occurrences have the following two patient characteristics in common: the patient is first exposed to hepatitis A and then is hospitalized (for other reasons) while in the prodromal period of hepatitis A infection when maximal fecal viral excretion (and communicability) is occurring; and the patient requires some type of nursing assistance with fecal hygiene for a variety of reasons including very young age, immobility, mental retardation, fecal incontinence, or diarrhea. Suboptimal handwashing efforts, hand (or other object)-to-mouth habits, or failure to use proper barrier precautions on the part of susceptible attendant staff then completes the chain of transmission.

A number of hepatitis A outbreaks also have occurred in neonatal intensive care units with several notable differences compared with ward outbreaks. First, the index infant care usually acquires...
hepatitis A virus via blood product infusion. Second, uniformly anicteric infection in neonates and a possibly prolonged period of fecal viral excretion often results in widespread secondary transmission to other neonates as well as staff persons.1–4

Prevention of such hepatitis A outbreaks falls upon routine adherence to basic infection control practices: in particular, precautions with feces or fecally contaminated articles. Because source patients are essentially never icteric or specifically diagnosed as having hepatitis A at the time of exposure of staff, the opportunity for timely use of immune globulin for prevention of the primary wave of staff cases rarely occurs. One or more hepatitis A vaccines will likely become available in the next several years15 but may only be routinely recommended for food handlers in the hospital setting.

HEPATITIS E

Hepatitis E virus is now the designation of the etiologic agent of enterically transmitted non-A, non-B hepatitis, also known as epidemic, fecal/oral, or waterborne non-A, non-B hepatitis. Large outbreaks of this type of hepatitis have occurred in southern Asia, north Africa, and most recently in two localized areas in Mexico.7 Transmission is most often waterborne. Relatively low secondary attack rates within households suggest that person-to-person spread is not an efficient mode of transmission of this virus.

However, healthcare workers attending patients must be considered potentially at risk for acquiring hepatitis E; a hepatitis attack rate of 42% was noted among expatriate medical staff working in Somali refugee camps during a hepatitis E outbreak, although the exact mode of acquisition of the virus by medical staff was not stated.17 Hepatitis E has not been reported in the United States except as an imported disease,18 and immune globulin produced in this country is not effective in preventing hepatitis E infection.17

HEPATITIS B

Numerous seroprevalence studies have documented an increased occupational risk of hepatitis B for healthcare workers who are exposed to blood or contaminated sharps.19,20 Such studies must always take into account nonoccupational risk factors for hepatitis B, such as race, as a recently published national serosurvey has documented a higher-than-expected prevalence of hepatitis B markers among African-Americans.21

The annual incidence of hepatitis B among healthcare workers in the United States was estimated by the Centers for Disease Control (CDC) to be 12,000 for 1987.22 This often-quoted figure probably needs to be updated for the 1990s. We have noted only one occupationally acquired hepatitis B infection (in a urologist) among healthcare workers in our 676-bed medical center in the last five years. Hepatitis B incidence among healthcare workers nationwide is likely decreasing because of increased reporting of exposure incidents (resulting in more consistent post-exposure management with hepatitis B vaccine and immune globulin), increased use of barrier precautions as part of Universal Precautions (which should decrease the rate of nonparenteral hepatitis B transmission), and increasing acceptance of hepatitis B vaccine among healthcare workers. A recent survey of staff at our institution showed that of 506 responding physicians and dentists, 72% had been vaccinated. The recently enacted Occupational Safety and Health Administration guidelines for protection of healthcare workers against bloodborne diseases will likely further significantly increase the number of healthcare workers vaccinated against hepatitis B.

Several issues relating to hepatitis B vaccination remain unresolved. These include the role of a vaccine booster dose, not only in healthcare workers who have lost detectable surface antibody since receipt of the primary vaccine series (hypo- or secondary nonresponders), but also in healthcare workers who are now five years or more out from their primary vaccine series but were never tested for surface antibody. There is also the problem of the 5% to 10% of healthcare workers who never develop hepatitis B surface antibody after vaccination (primary nonresponders) and therefore remain unprotected. Experimental hepatitis B vaccines that incorporate pre-S epitopes hold some promise for increased immunogenicity and protective efficacy for such hypo- or nonresponders to currently available vaccines.23

For persons who have responded to hepatitis B vaccine, a disconcerting new development is the occurrence of a “vaccine-escape” mutant hepatitis B virus variant strain with an altered hepatitis B surface antigen (HBsAg) determinant that is only partially neutralized by the surface antibody induced by plasma-derived hepatitis B vaccine.24 Infection with this mutant strain has thus far only been described in a relatively few vaccinated patients in Italy, but this development suggests that future hepatitis B vaccines may need to include “mutant” surface antigen if such hepatitis B virus variants become widespread.

HEPATITIS D

Hepatitis D virus, formerly called the Delta agent, may infect healthcare workers as a coprimary infection with hepatitis B virus (co-infection) or may infect healthcare workers who are already carriers of hepatitis B virus (super-infection). Transmission of
hepatitis D to healthcare workers via needlestick injury and via nonparenteral exposure in a dialysis unit has been reported.\textsuperscript{23} Hepatitis D infection is likely underreported as a problem in healthcare workers because co-infection with hepatitis B is usually clinically indistinguishable from infection with hepatitis B alone, and because hepatitis D antibody testing is often not routinely done.

Prevention of hepatitis B/D co-infection will be accomplished via successful vaccination and other measures that prevent primary hepatitis B infection. Prevention of hepatitis D in the estimated 1% of healthcare workers who are already carriers of hepatitis B, is problematic. No biologic product is currently available for pre-exposure or postexposure prophylaxis of hepatitis D in healthcare workers who are already HBsAg-positive. Prevention of hepatitis D infection must rely on avoidance of injury by contaminated sharps and on strict adherence to other appropriate barrier precautions. An emerging option is α-interferon or other antiviral therapy of chronic hepatitis B in an attempt to resolve the carrier state.\textsuperscript{26}

**Hepatitis C**

Multiple studies now have confirmed that hepatitis C virus (HCV) is the major etiologic agent of community-acquired non-A, non-B hepatitis in the United States and parenterally transmitted non-A, non-B hepatitis worldwide.\textsuperscript{27,28} An enzyme immunoassay (EIA) test for an anti-HCV antibody directed at a nonstructural HCV protein antigen (C-100) became commercially available in the United States in May 1990. While useful as a screening test for chronic active HCV infection to further decrease the risk of posttransfusion hepatitis, the C-100-based EIA test for HCV antibody has a low sensitivity for the diagnosis of both acute HCV infection and past (resolved) HCV infection. In addition, as is the case with many screening tests, it has low positive predictive value in populations with a low prevalence of HCV infection, such as asymptomatic volunteer blood donors.

Further research has discovered additional HCV antigens that have been incorporated into multi-antigen “second generation” HCV supplementary (“confirmatory”) tests that detect multiple HCV antibodies.\textsuperscript{30} These newer assays significantly enhance the sensitivity and specificity of HCV testing. Supplementary testing is currently available on request from the manufacturers of the currently available EIA test kits and will likely become commercially available sometime in 1992.

Testing of healthcare workers for HCV antibody is now beginning to shed further light on the magnitude of the occupational risk of HCV for healthcare workers. The article by Cooper et al in this issue of Infection Control and Hospital Epidemiology\textsuperscript{31} reports the results of HCV testing of a group of healthcare workers at high risk of previous blood exposure. The seroprevalence of HCV antibodies (confirmed by a second-generation assay) in this group was only 1.6%, a low rate comparable with the 0.5% to 1.5% rate found in voluntary blood donors and in the range of rates of 1.2% to 2.8% reported in other studies of unselected healthcare workers.\textsuperscript{32,34} It is somewhat surprising that the HCV seroprevalence rate found by Cooper et al in their subset of high-risk personnel was not increased analogous to the higher hepatitis B marker seroprevalence previously described in such groups. Additional studies are needed to confirm their findings. Although HCV antibody screening by the C-100-based EIA test may miss, and thus underestimate, past (resolved) HCV infection in healthcare workers, this lack of test sensitivity should apply equally to studies of volunteer blood donors so that the comparability of the low seroprevalence rates in these two groups should remain valid.

Although seroprevalence studies have not yet found a significantly increased risk of HCV for healthcare workers, occupational transmission of non-A, non-B hepatitis virus (HCV) via needlestick injury has been suggested by anecdotal reports in the past.\textsuperscript{35,36} Such transmission has now been much better documented by specific HCV testing of source patients and exposed healthcare workers.\textsuperscript{37-40} Three of these studies are case reports that documented HCV seroconversion of a nurse,\textsuperscript{38} a dialysis nurse,\textsuperscript{39} and a surgeon\textsuperscript{40} in conjunction with hepatitis occurring six weeks, five weeks, and four weeks, respectively, after the needlestick exposure. The source patients for the nurses tested positive for HCV, while the source patient for the surgeon, although not tested for HCV, was a parenteral drug abuser (a known high-risk group for HCV infection).

In the only large study of needlestick transmission of HCV reported to date, where both the source patients were documented to be HCV-positive and the exposed healthcare workers had serial liver function testing and serologic follow-up, the rate of transmission was low.\textsuperscript{35,36} Of 110 such HCV-exposed healthcare workers, only four developed hepatitis, and only three of these seroconverted to HCV antibody-positive-a needlestick transmission rate for HCV that is intermediate between the rates for hepatitis B and human immunodeficiency virus. The most likely explanation for this low needlestick transmission efficiency of HCV is the low concentration of this virus in the blood of chronically infected patients.

Although the overall risk of HCV for healthcare workers appears to be low, HCV is a virus to be taken seriously. Approximately 50% of persons who are
infected via blood transfusion or who acquire infection in the community setting become HCV carriers. A significant proportion of HCV carriers will develop chronic liver disease with the attendant long-term risk of cirrhosis and primary hepatocellular carcinoma. Because there is not yet any consistently effective antiviral treatment of HCV, prevention of infection is very important.

However, the effectiveness of immune globulin in the postexposure prevention of non-A, non-B virus (HCV) has not been established, although its administration after needlestick exposure to non-A, non-B hepatitis has been suggested by the CDC, at least pending data on efficacy (or lack thereof). 41 The antibodies detected by current HCV assays are not neutralizing and thus do not protect against HCV. Whether immune globulin contains HCV neutralizing antibodies cannot yet be determined, and the identification of such antibodies represents a major research priority in the control of HCV. It is of note that two 10 ml doses of immune globulin given to a healthcare worker after a needlestick exposure has failed to prevent transmission of HCV on at least one occasion. 42

Another controversial issue is the appropriate use of HCV testing in the evaluation of patients who are the source of exposures to healthcare workers. No clear answers are yet available. The positive predictive value of commercially available tests for HCV antibody would likely be higher in a hospitalized patient population than in volunteer blood donors, but both false-positive and false-negative results would still be a problem. Selective testing of high-risk sources such as parenteral drug abusers, multiply-transfused persons, or patients with unexplained liver enzyme abnormalities would improve the test characteristics but would require subjective judgments about the clinical history and laboratory results of patients. Second-generation HCV antibody assays will improve test sensitivity for active infection but may detect more persons with resolved HCV. A practical assay for circulating HCV antigen that would define infectivity, analogous to HBsAg for hepatitis B virus, is urgently needed. Circulating HCV RNA has been detected by the polymerase chain reaction but that technology still remains primarily a research tool. 42

REFERENCES


