

HEPATITIS VIRUSES A, B, C, D, E AND G: IMPLICATIONS FOR DENTAL PERSONNEL

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In the last 33 years, six distinct viruses have been identified as causing viral hepatitis. These viruses are labeled A, B, C, D, E and G. A review of reports of acute viral hepatitis cases in the United States from 1982 through 1995 indicates that 48 percent were caused by hepatitis A virus, or HAV; 34 percent by hepatitis B virus, or HBV; 15 percent by hepatitis C virus, or HCV; and 3 percent by hepatitis of a strain other than A through E.¹ Furthermore, there are patients with common symptoms of acute viral hepatitis who do not have serologic markers for any of the known viruses; hence, it is presumed that another virus or other viruses responsible for hepatitis remain unidentified.¹

There are four compelling reasons why dental

ABSTRACT

Background. This article provides dental personnel with a brief overview of the different types of viral hepatitis, including their epidemiology, clinical features, prevention and treatment. It also explores the ramifications of these diseases for the practice of dentistry.

Description of the Condition. Viral hepatitis is an inflammation of the liver caused by one of at least six distinct viruses. The hepatitis A and E viruses, or HAV and HEV, are enterically transmitted viruses that produce acute disease only. The hepatitis B, C and D viruses, or HBV, HCV and HDV, are most efficiently transmitted by infected blood, but also can be transmitted by exposure to other infectious bodily fluids. These three viruses can cause acute or chronic hepatitis. People with chronic viral hepatitis can develop chronic liver disease, cirrhosis and hepatocellular carcinoma. The hepatitis G virus was recently identified, and its ability to cause clinically significant acute or chronic hepatitis is unknown.

Conclusions. Dental health care workers, or DHCWs, should be concerned primarily with HBV, HCV and HDV, as occupational exposure to these pathogens places them at risk of developing acute or chronic infections. Vaccines and immune globulins are available and effective in protecting against infections with HAV, HBV and HDV, but not HCV.

Clinical Implications. DHCWs should become knowledgeable about viral hepatitis. They should be vaccinated against hepatitis B. Adherence to infection control measures will help prevent occupational transmission of all bloodborne pathogens, including hepatitis viruses.

professionals should familiarize themselves with hepatitis viruses:

- the viruses are prevalent worldwide;
- most of the viruses are associated with significant morbidity and mortality;
- occupational transmission of bloodborne types can occur in dental settings;
- specific preventive measures—including immunoprophylaxis, lifestyle modification and infection control—afford protection against acquiring these diseases.

HEPATITIS A VIRUS

“Epidemic jaundice” was described in Babylonian, Greek and Roman literature in about the fifth century B.C. and in Chinese literature around A.D. 200.² Historical accounts of probable hepatitis A outbreaks associated with troops engaged in military

campaigns and among civilians were documented by various investigators from the Middle Ages through the 20th century.¹ However, it was not until 1973 that Battegay and Feinstone³ visually identified the virus by immune electron microscopy.

HAV is a nonenveloped (naked) spherical particle with a diameter of 27 to 28 nanometers. It is an enterovirus of the Picornaviridae family, and its genome is composed of single-stranded ribonucleic acid, or RNA.⁴ HAV produces either asymptomatic or acute symptomatic infection that ranges in severity from mild to fulminant. Each year, approximately 100 Americans die of fulminant hepatitis A. The case fatality rate among Americans of all ages is 0.3 percent, but for adults older than 50 years of age, the risk of death resulting from hepatitis A is 1.8 percent.⁵ Usually, the clinical course of hepatitis A is self-limiting, with most patients experiencing full recovery, no chronic liver disease and lifelong immunity to the disease. HAV replicates in the liver, is excreted in bile and is shed in the stool.³ Transmission occurs when virus shed in the feces of an infected person is ingested by a susceptible person. The average incubation period after exposure is 28 days (range: 15-50 days).⁶ The highest rates of transmission in the United States occur among children 5 to 14 years of age.⁵

As most young children with HAV are asymptomatic, they serve as an inconspicuous reservoir of infection for susceptible adults.⁷ The predominant mode of HAV transmission in the United States is close personal contact.⁵ As many as 42 percent of the cases are attributed to

household, sexual and day-care-center contact with an infected person. Between 4 and 6 percent of cases occur among travelers to HAV-endemic countries, and 3 percent are related to ingestion of contaminated food or water. The source of infection for the remaining HAV cases among Americans is unknown.

HAV can be found in the blood of infected people during the same period when virus is being shed in the stool, and transfusion-related HAV infec-

There is no evidence that hepatitis A viremia poses an occupational risk to dental personnel as a result of percutaneous injury.

tions have been documented but are rare.^{8,9} There is no evidence that HAV viremia poses an occupational risk to dental personnel as a result of percutaneous injury. HAV has also been detected in the saliva of a chimpanzee orally inoculated with HAV; however, there is no evidence of transmission by saliva.⁹

HAV has a global distribution, but in comparison with developing countries, the United States has low levels of HAV endemicity owing to its clean water supplies, good sewage disposal and socioeconomic conditions. However, 67 percent of the American population is susceptible to HAV, and community-wide outbreaks are common.^{7,10} Over the last 44 years in this country, large epidemics of HAV have occurred approxi-

mately once each decade (1954, 1961, 1971 and 1989).⁶ Since 1989, there has not been a major nationwide outbreak. However, between epidemics, hepatitis A continues to occur at high rates. The Centers for Disease Control and Prevention estimates that 125,000 to 200,000 infections occur annually in the United States.¹¹ Consequently, HAV remains a major public health problem, primarily because of its morbidity and the costs of providing medical care, hospitalization, pre-exposure and postexposure prophylaxis, and coverage for work loss.⁵

Protection against HAV infection. Effective products are available to protect people from HAV infection. HAV-immune globulin, made from pooled plasma, has been used since its effectiveness was first demonstrated more than 50 years ago.¹² This form of passive immunization is 90 percent effective in preventing HAV infection and can be administered either before anticipated exposure or within two weeks after exposure early in the incubation period.^{6,13}

In February 1995, with the advent of licensed HAV vaccine, active immunization against HAV became a reality. Two vaccines (HAVRIX by SmithKline Beecham Pharmaceuticals and VAQTA by Merck & Co.) containing formalin-inactivated virus have proven to be safe, highly immunogenic and effective in preventing HAV infection in clinical trials.¹⁴ The immunogenic response to the vaccine among adults and children is so high that postvaccination testing is not necessary.⁵ In theory, widespread vaccination will reduce the pool of sus-

ceptible people, prevent community-wide outbreaks and lead to eradication of the disease.⁷

Licensed vaccines are not currently approved for administration to children younger than 2 years of age. Until they are, the Advisory Committee on Immunization Practices, or ACIP, of the U.S. Public Health Service recommends vaccinating groups at increased risk and communities with high rates of HAV.⁵ People at increased risk include international travelers, homosexuals and bisexuals, users of injected drugs, people with chronic liver disease and those whose occupation places them at risk.

Active immunization of dental personnel with HAV vaccine is not indicated, as occupational exposure does not increase a health care worker's, or HCW's, risk of developing HAV infection except in specific settings.^{5,15} Populations in the United States with high rates of infection include American Indians, Alaskan natives, Pacific Islanders, and some Hispanic and religious groups.⁵ The approach of immunizing only those at high risk has had very limited effectiveness in reducing the incidence of HBV, and it is predicted that little reduction in the overall incidence of hepatitis A will be achieved without a strategy of universal childhood immunization.^{5,7,8,14}

Before traveling to developing countries on vacation or to perform dental missionary work, people susceptible to HAV should receive hepatitis A vaccine or immune globulin. The first dose of vaccine should be administered at least four weeks before departure to ensure that a protective level (greater than 20 milli-

national Units per milliliter) of antibodies (anti-HAV) is established. The second immunization should be administered six to 12 months later for long-term protection.⁵

HEPATITIS E VIRUS

The virus that causes hepatitis E, or HEV, was first identified in 1983 and is a nonenveloped, icosahedral virus 27 to 34 nm in diameter.¹⁶⁻¹⁸ HEV has a genome composed of a single-stranded RNA molecule. It structurally resembles viruses of the Caliciviridae family, but its exact scientific classification is yet to be determined.^{17,19} The route of transmission of HEV, like that of HAV, is fecal-oral; however, the predominant vehicle of transmission of HEV is fecally contaminated drinking water.

HEV occurs primarily in developing countries with inadequate environmental sanitation and unsafe drinking water supplies.¹⁹ Safe drinking water standards make hepatitis E an extremely rare infection in the United States and other industrialized nations. Cases reported among U.S. residents are infrequent and have been associated with a recent history of international travel.²⁰ The incubation period for HEV ranges from 15 to 60 days, with the mode being 40 days.¹⁷ The highest rates of clinically evident disease occur in people 15 to 40 years old.¹⁹ HEV infection has a self-limited course and does not cause chronic hepatitis²¹; nevertheless, it is a serious infection because of high case fatality rates (0.5 to 3 percent).¹⁷ Pregnant women infected with the virus are particularly vulnerable to fulminant hepatitis and experience case fatality

rates of 15 to 25 percent.¹⁷ The development of protective immunity after active infection has not been ascertained.^{17,19}

No effective immunoprophylaxis for HEV exists. Prophylactic use of immune globulin has proven ineffective in preventing HEV infection. While a vaccine has yet to be developed that confers protection, progress toward one in preliminary animal studies looks promising.^{14,16,17,19}

Protection against HEV infection. People traveling to HEV-endemic regions can reduce their risk of infection by taking the following actions¹⁷:

- not drinking water or beverages mixed with water or served with ice;
- avoiding the consumption of raw fruits and vegetables that have been contaminated by handling or that have been rinsed with water;
- not eating uncooked shellfish that may have been harvested from polluted waters.

HEPATITIS B VIRUS

In 1963, geneticist Baruch Blumberg discovered an unknown antigen he termed "Australia antigen" in the blood of an Australian aborigine.^{2,22} Subsequent investigation revealed that the antigen, now known as hepatitis B surface antigen, or HBsAg, actually was the surface component of HBV and a serologic marker for HBV infection.^{2,22} Identification of the three particle types of the virus by electron microscopy was first described in 1966.² Since that time, a number of developments have occurred:

- diagnostic assays for HBV have been developed;
- the virus' epidemiology and modes of transmission have

been thoroughly investigated;

- safe and effective vaccines have been developed, tested and administered around the world;
- a comprehensive strategy for eliminating HBV transmission in the United States through universal vaccination of newborns is progressing;
- global elimination of HBV through vaccination has become a pursuable goal.

HBV is a 42-nm virus of the Hepadnaviridae family. The HBV genome is composed of partially double-stranded circular DNA.²³ The virus has an inner core containing hepatitis B core antigen, or HBcAg, and hepatitis B e antigen, or HBeAg. HBeAg is produced during replication, circulates in the blood and is associated with greater HBV infectivity.²³ The envelope of the virus contains HBsAg, which is the principal component of the hepatitis B vaccine.¹⁴

The incubation period for HBV is 45 to 160 days, with the average being 120 days.²⁴ Most infants and young children with acute disease are asymptomatic, with less than 10 percent of them exhibiting jaundice. Nevertheless, the younger the person is at the time of infection, the higher his or her risk of developing chronic HBV infection.²⁵ Among older children and adults with acute infection, 30 to 50 percent exhibit clinical illness with jaundice, yet most completely recover and then are immune to the virus. Case fatality rates associated with acute infection among Americans are 0.5 to 1 percent.^{26,27} Chronic infection develops in 5 to 10 percent of adults, 25 to 50 percent of children aged 1 to 5 years and 90 percent of infants infected with HBV.²⁵

The highest rates of the disease in the United States occur in young adults 25 to 39 years of age.²⁸

Prevention of chronic infection is a primary concern in HBV because of its severe consequences. The magnitude and severity of the problem is immense if one considers its global profile. About 45 percent of the world's population resides in countries with a high prevalence of chronic HBV infection. Worldwide, 300 to 350 million people are chronically infected.²¹ In general, the prevalence of HBV in the United States is low, although there are children in specific racial/ethnic groups—Alaskan natives, Pacific Islanders and first-generation immigrants from countries of high endemicity—with high rates of infection.⁶ CDC estimates that in the United States, 1 to 1.25 million people are chronically infected with HBV; 140,000 to 320,000 new infections occur each year; and 5,000 to 6,000 deaths occur annually as a result of chronic liver disease, including liver cancer associated with chronic HBV infection.²⁹

HBV is efficiently transmitted by percutaneous and per-mucosal exposures; however, the most frequent route of transmission in the United States is by high-risk sexual activity.^{6,23,24} Bodily fluids that can cause HBV infection (as evidenced by inoculation into non-human primates) include blood, semen, vaginal fluids and saliva.^{30,31} A thorough investigation of a teacher whose finger was accidentally bitten by a student demonstrated that HBV can be transmitted by infectious saliva in human bite wounds.³² However, mucosal exposure

(oral and nasal) to infectious saliva does not produce infection, suggesting that kissing poses little risk.³¹⁻³³

Percutaneous exposure to infectious blood can occur in several ways: sharing of contaminated needles by users of injectable drugs, hemodialysis, multiple transfusions of blood and blood products, organ or tissue transplantations, tattooing, acupuncture, body piercing, sharing of razors and occupational injury of HCWs by contaminated sharps.²¹ The highest HBV infection rates among HCWs are found in dentists and oral surgeons.³⁴ A study of dentists and oral surgeons recruited at national dental meetings indicated that about 8 percent of general dentists and 21 percent of oral surgeons had serologic markers for HBV infection.³⁴ The risk of seroconversion for a nonimmune HCW after a needle-stick exposure with HBV-infected blood ranges from 2 to 40 percent, depending on the presence of HBeAg in the blood.³⁵ Mucosal exposures can occur by heterosexual or homosexual contact with infected partners, as well as perinatally when infants' mucous membranes are exposed to infected maternal blood.

Protection against HBV infection. The HBsAg is the component of the vaccine that induces production of neutralizing antibodies known as anti-HBs. Antibody titers at or above 10 mIU/mL in the circulating blood are considered to be protective.³⁶ The first vaccine to confer immunity against hepatitis B, Heptavax, was developed by Merck, Sharp & Dohme in 1981. Although this vaccine was safe and highly effective, the fallacious perception of its po-

tential for inducing HIV contamination is thought to have discouraged some providers from being vaccinated. One study of the vaccine found it to be 86 percent effective in producing protective antibodies in dental personnel 23 to 75 years old.³⁷ These findings did not take into account the site of vaccine inoculation.

Plasma-derived vaccines have largely been replaced by recombinant vaccines (Recombinax HB by Merck, Sharp & Dohme and Engerix-B by SmithKline Beecham Pharmaceuticals) derived from HBsAg synthesized from yeast. The vaccine is given in a series of three injections and should be administered intramuscularly (in the deltoid muscle of adults and children, and in the anterolateral thigh muscle of infants), with a needle 1 to 1.5 inches long.^{15,24} If administered properly, it induces immunity in 95 to 99 percent of infants, children and adolescents and in more than 90 percent of healthy adults.²⁴ Immunogenic responses to the vaccine are lower in adults who are older than age 40 years, are immunocompromised, are obese or smoke.^{37,38} Approximately 33 to 50 percent of those who have no response or inadequate response to the primary series produce a protective antibody response after two or three additional doses.³⁶

Merck & Co. also has developed a combined hepatitis B (recombinant) and *Haemophilus influenzae* type b, or HIB, conjugate vaccine (COMVAX) for infants, which was licensed by the U.S. Food and Drug Administration in October 1996.³⁹

In one study of U.S. dentists in which demographic, seroprevalence and questionnaire

data from annual health screenings were analyzed, the percentage of dentists reporting hepatitis B vaccination increased markedly from 22 percent in 1983 to 85 percent by 1992.⁴⁰ In 1992, immunization was reported by 93 percent of dentists who had been in practice less than 10 years. This same study revealed that dentists who had not been vaccinated were five times more likely to be HBV-infected than those who had received the vaccine.

An attempt to eliminate HBV infection through selective vaccination of high-risk groups has had limited success. However, among HCWs who were vaccinated, a 95 percent reduction in incidence of disease occurred from 1983 to 1995.⁴¹ Before vaccination of HCWs in the mid-1980s, the rate of HBV infection resulting from occupational exposure was three times higher than the incidence in the general population. By 1995, dramatic declines in disease rates to a level five times lower than the incidence in the general population occurred among HCWs, owing to wide-scale vaccination and adherence to universal precautions.^{6,41} Today, HCWs are at much lower risk of HBV infection than the general population. Current recommendations for elimination of HBV transmission in the United States include the following:

- screening pregnant women for the HBsAg to identify newborns who will require prophylaxis to prevent perinatal infections;
- routine vaccination of infants and children 11 to 12 years old who had not previously been vaccinated; vaccination of high-risk groups; and screening people who will donate their blood,

organs or tissues.^{24,42}

Long-term vaccine protection. Mahoney identified 10 long-term studies of 1,786 people at high risk of acquiring HBV infection who responded immunologically to the primary vaccine series. Many of these respondents experienced a decline in antibody titer below optimal levels over a period of five to 11 years. Despite this finding, only a few people experienced mild, subclinical infections as evidenced by anti-hepatitis B core, and none developed chronic HBV infection.⁴¹ It appears that immune memory remains despite a decline in antibody titer, an occurrence referred to as "anamnesic response." Consequently, ACIP does not recommend booster doses of vaccine for those who are known to have responded to the primary vaccine series.¹⁵ HCWs who have contact with patients or blood should undergo postvaccination testing one to two months after completion of the vaccination series to determine the adequacy of their immunogenic response.¹⁵ This information is useful when managing postexposure incidents.

Hepatitis B immune globulin, or HBIG, also effectively provides temporary protection (for three to six months) against HBV and is used only in postexposure situations defined as percutaneous or mucous membrane exposure to known or suspected infectious blood.^{15,24} For specific postexposure prophylaxis to HBV, dental personnel are advised to follow ACIP's most current recommendations.¹⁵

HEPATITIS D VIRUS

In 1977, Dr. Mario Rizzetto discovered hepatitis D virus, or

HDV, in liver cell nuclei and serum of patients who were carriers of HBV and had chronic liver disease.⁴² HDV is a spherical virus 35 to 40 nm in diameter.^{18,43} It is a defective virus whose survival, replication and infectivity depend on the presence of HBV. Hepatitis D requires the help of HBV to produce an envelope of HBsAg.⁴⁴ The HDV genome (single-stranded RNA) and the delta, or D, antigen are packaged within this HBsAg coat.⁴⁵

Animal inoculation studies have demonstrated that HDV infections are either coinfections or superinfections.^{43,44} When HDV infection is acquired simultaneously with HBV, it is termed an HBV-HDV coinfection. Coinfections are often associated with a higher occurrence of fulminant hepatitis than infection by HBV alone.⁴⁶ Globally, 3 to 25 percent of fulminant hepatitis B cases are actually coinfections with HDV.⁴³ Coinfections generally are self-limiting, and there is a low risk (less than 5 percent) of developing chronic hepatitis from these types of infections, because as the patient eliminates the HBV, HDV cannot survive.^{23,45,47}

Superinfections occur when chronic hepatitis B carriers subsequently become infected with HDV. Seventy to 95 percent of patients with superinfections become chronically infected with both viruses.^{23,45} Progression to cirrhosis occurs in 70 to 80 percent of patients who have chronic hepatitis D.⁴⁵

HDV's incubation period after exposure is 15 to 150 days, with an average of 35 days.⁴⁵ HDV's clinical course is highly variable and depends on several factors, including geographic location, route of transmission,

type of infection (coinfection or superinfection), age of patient and strain of virus.⁴³ The prevalence of HDV in the United States is low and parallels the low prevalence of chronic HBV.²¹ CDC estimates that about 7,500 HDV infections occur annually.⁵ Approximately 1,000 people die each year in the United States as a result of chronic liver disease associated with chronic hepatitis D.

The HDV virus can be transmitted by percutaneous and permucosal routes; however, percutaneous exposures are the most efficient mode.^{45,48} The HDV infections in the United States occur most commonly in users of injectable drugs and in hemophiliacs who receive multiple transfusions of pooled plasma products.²¹ Because HDV depends on the presence of HBV to cause infection, strategies to eliminate transmission of hepatitis B through routine newborn and childhood vaccination programs also should eliminate HDV transmission.²⁴ Compliance with hepatitis B vaccination programs has been excellent among dentists and other HCWs, placing them at very low risk of developing HDV.^{15,26,41}

Protection against HDV infection. As mentioned above, immunization with the hepatitis B vaccine also confers protection against coinfections with HDV-HBV. Either pre- or postexposure prophylaxis using vaccine and hepatitis B immune globulin can prevent coinfections. Currently, there is no product available to protect hepatitis B carriers from superinfections with HDV. Prevention of superinfections in this group relies entirely on modification of risky behaviors.

HEPATITIS C VIRUS

HCV, the primary cause of parenterally transmitted non-A, non-B hepatitis known to exist since the early 1970s, was first identified through molecular cloning techniques in 1988.^{49,50} It is an enveloped virus estimated to be between 40 and 50 nm in diameter with a positive-strand RNA genome that is related to viruses of the Flaviviridae family.^{23,51} At least six major strains, or genotypes, and more than 80 subtypes, or quasi-species, of HCV have been identified globally.⁵²

The incubation period after exposure to HCV is 15 to 150 days, with an average of 50 days.⁵² Because the clinical course of the disease is generally insidious, mild and slow to progress, most patients are unaware they are infected. Among people with acute infections, 70 to 80 percent are asymptomatic and anicteric; the remainder develop clinical disease with jaundice.^{53,54} The highest incidence of disease occurs among young adults 20 to 39 years of age with high-risk lifestyles.⁵⁵

Hepatitis C may be the most serious of the viral hepatitis infections because of its ability to produce chronic infection. Only 15 percent of those with acute infection recover, while 85 percent become chronically infected with long-term vulnerability to cirrhosis, hepatocellular carcinoma and liver failure.^{28,54} Sixty to 70 percent of chronically infected people develop active liver disease.⁵⁵ HCV is now the leading cause of liver transplantation in the United States.^{54,56} The inability of most people to clear the virus after acute infection is believed to be a result of mutant variants produced that

escape detection by the host's immune system.⁵² Consequently, development of neutralizing antibodies to HCV (anti-HCV) after acute infection offers little, if any, protection.⁵⁷

It is estimated that nearly 4 million people in the United States are infected with HCV. Currently, 30,000 new infections occur each year; however, the annual incidence of HCV infections has decreased dramatically since 1989, owing perhaps to safer needle-use practices among users of injectable drugs.^{55,58} In the United States, 8,000 to 10,000 people die each year of chronic liver disease related to chronic infection with HCV.⁵⁴ The number of deaths is expected to triple over the next two decades if effective preventive strategies are not developed and implemented.⁵⁴

Direct percutaneous exposure to infected blood is the most efficient mode of transmission of HCV.⁵⁸ Per mucosal exposure to infectious bodily secretions is a documented, but less effective, route of transmission. Risk factors for HCV in the United States include use of injectable drugs, transplantation of organs or tissues, transfusions of blood or blood products, accidental injuries from contaminated sharps, hemodialysis, household contacts, sexual activity and perinatal exposure.⁵⁸

The incidence of posttransfusion hepatitis C before 1986 was 5 to 13 percent. After identification of the virus and with the development of diagnostic tests (first- and second-generation enzyme immunoassays as well as supplementary recombinant immunoblot assays) to screen blood donors for antibodies (anti-HCV) to hepatitis C,

the incidence of posttransfusion HCV has been significantly reduced, to levels as low as 0.1 percent.^{58,59} Furthermore, one study confirmed that the overall rate of HCV infection among U.S. blood donors was low, with less than 0.4 percent showing seropositivity.⁶⁰

It has been reported that hepatitis C can be sexually transmitted to heterosexual partners of HCV-infected patients.⁶¹ Consequently, sexually active heterosexuals with multiple partners are at increased risk of contracting HCV. Use of injectable drugs accounts for approximately 60 percent of HCV infections in the United States.⁶²

Risks of occupational transmission of HCV.

Annually, 2 to 4 percent of new HCV infections occur among HCWs.¹⁵ The first known case of occupational mucosal transmission of HCV involved a nurse who was splashed in the face and eyes by blood.⁶³ HCV also has been detected in the saliva of patients with chronic hepatitis who are undergoing dental treatment,⁶⁴ and there is a report of HCV being transmitted by saliva in a human bite.^{64,65}

Studies assessing the occupational risk of contracting HCV among dentists in the United States, Taiwan and Wales have shown conflicting findings. A study by New York City researchers found that 9 percent of oral surgeons vs. about 1 percent of all other categories of dentists had anti-HCV antibodies to hepatitis C compared with only 0.14 percent of a control group of blood donors.⁶⁶ Another U.S. study found that 2 percent of oral surgeons vs. 0.7 percent of general dentists tested positive for anti-HCV anti-

bodies.³⁴ Three of the four studies show that the risk of HCV infection through the practice of dentistry generally is low.^{34,67,68} The incidence of seroconversion of an HCW after needle-stick exposure to HCV-infected blood ranges from 0 to 10 percent and averages about 2 percent.^{58,69-71}

Protection against HCV infection. Currently, there is no vaccine for HCV, and the chance of developing one is complicated by the virus' diversity and ability to mutate.⁵² For similar reasons, hepatitis C immune globulin, unlike hepatitis A and hepatitis B immune globulin, does not provide effective postexposure prophylaxis, and its use is not recommended.^{28,57}

Postexposure recommendations for HCV. In the event an HCW sustains a percutaneous or permucosal exposure to blood, the source person should be tested for HCV, and the exposed worker should receive baseline and follow-up testing for anti-HCV and alanine aminotransferase, or ALT, activity. Enzyme immunoassay is used to diagnose HCV infection, as are supplemental confirmatory tests such as recombinant immunoblot assay and reverse transcriptase polymerase chain reaction, or RT-PCR, assays. Postexposure prophylaxis with immune globulin or antiviral agents such as interferon- α , or IFN- α , is not recommended because immune globulin is ineffective and guidelines for use of antiviral agents for acute HCV infections have not been established.^{62,71}

HEPATITIS G VIRUS

Two independent groups of investigators discovered, hepatitis G virus, or HGV, in 1995, and the virus was fully character-

ized in 1996.⁷²⁻⁷⁴ HGV is a positive, single-stranded RNA virus of the Flaviviridae family.⁷⁵ Isolates of HGV from different geographic regions indicate that there are specific genotypes and subtypes of the virus.⁷⁵ HGV's modes of transmission and risk factors have not been fully investigated; however, it clearly is a bloodborne virus that frequently occurs as a coinfection with other bloodborne or enterically transmitted hepatitis viruses. In a recent study, serum samples available from a subgroup of patients identified through CDC's sentinel counties viral hepatitis surveillance system were tested for HGV RNA.¹ HGV was detected in 25 percent of patients with hepatitis A, 32 percent of patients with hepatitis B, 20 percent of patients with hepatitis C, and 9 percent of patients with hepatitis not of the A, B, C, D or E strains.¹ It is estimated that of all acute cases of viral hepatitis in the United States, only 0.3 percent may be infections of HGV alone.¹

Documented routes of HGV infection have occurred by experimental inoculation of non-human primates, transfusions and perinatal transmission.^{1,72,73,75-77} Until a simple diagnostic test to screen the blood for antibodies to HGV (anti-HGV) becomes commercially available, it will be difficult to study its epidemiology, including its prevalence in the general population.¹ The technique currently being used to diagnose HGV infection is PCR, which detects viral RNA in serum, tissues and fluids, but does not detect evidence of past infections.^{75,78} Notably, 1 to 2 percent of U.S. blood donors test seropositive for HGV RNA, but

they are not representative of the general population, among whom the prevalence is predicted to be even higher.^{1,73,75,76}

Although there is evidence to show that HGV is transmissible by percutaneous and perinatal exposures to blood, there is no evidence to indicate whether permucosal exposures play any role. HGV may be a non-pathogenic form of viral hepatitis, because infection produces persistent viremia without evidence of acute or chronic hepatitis.^{1,75,78} The identification of HGV is so recent an event that its epidemiology—including risk factors and modes of transmission, prevention, treatment and clinical evidence of disease—has yet to be established.

TREATMENT OF CHRONIC HEPATITIS

IFN- α is currently the most effective treatment for patients with chronic viral hepatitis. A meta-analysis of 15 randomized controlled trials was conducted to examine the efficacy of IFN- α for treatment of patients with chronic hepatitis B infection.⁷⁹ The analysis revealed that three to six months of treatment with IFN- α was effective in terminating viral replication (HBeAg) in 33 percent of treated patients vs. 12 percent of untreated control subjects; eliminating HBV DNA in 37 percent of treated patients vs. 17 percent of control subjects; and eliminating the carrier state (HBsAg) in 8 percent of treated patients vs. 2 percent of control subjects.⁷⁹ Loss of HBeAg and HDV DNA from serum with a return to near-normalization of serum aminotransferase is generally indicative of successful treatment.⁸⁰

Treatment of chronic HDV

has proven to be disappointing and quite challenging because of the tendency of patients to experience relapse after therapy is discontinued.⁴⁵ Low doses of interferon are ineffective, showing only transient benefits in biochemical or virologic response.^{45,81} High doses of IFN- α administered over the long term result in sustained improvement in 15 to 25 percent of patients.⁸⁰ One study conducted at the National Institutes of Health revealed that chronic HDV infection in patients resolves after clearance of HBsAg from serum.⁸² In this study, only 17.5 percent of patients receiving doses of 5 million units of IFN- α daily for an average of 11.6 months lost HBsAg and had sustained clearance of HDV RNA.⁸² Antiviral therapy incorporating nucleoside analogues like lamivudine and famciclovir may hold promise for future treatment of chronic HBV and HDV.^{45,83,84} The use of lamivudine for treatment of chronic hepatitis B is under consideration by the FDA.

Treatment of chronic hepatitis C using the standard six-month regimen of IFN- α 2b has been successful in producing a sustained response—defined as normalization of serum ALT levels and loss of serum HCV RNA six months after therapy—in only 10 to 20 percent of patients.^{52,54,80,85} Prolonged therapy for 12 months or longer has shown better sustained response rates of 20 to 30 percent and is now recommended.^{54,86} Researchers also are evaluating the effectiveness of an improved sustained response rate in patients to combination therapy for hepatitis C using both IFN- α and an antiviral drug called ribavirin. Recent reports indicate

TABLE

SUMMARY OF HEPATITIS VIRUSES.						
VIRUS TYPE	B	A	D	E	C	G*
YEAR IDENTIFIED	1966	1973	1977 [†]	1983	1988	1995-1996
APPROXIMATE DIAMETER (NANOMETERS)	42	27 to 28	35 to 40	27 to 34	40 to 50	Unknown
SOURCE	Blood and other bodily fluids	Feces	Blood and other bodily fluids	Feces	Blood and other bodily fluids	Blood
MODE(S) OF TRANSMISSION	Percutaneous/per mucosal	Fecal-oral	Percutaneous/per mucosal	Fecal-oral	Percutaneous/per mucosal	Percutaneous
INCUBATION PERIOD	45 to 160 days, average 120 days	15 to 50 days, average 28 days	Presumed comparable to that of hepatitis B (15 to 150 days, average 35 days)	15 to 60 days, mode 40 days	15 to 150 days, average 50 days	Unknown
RISK OF CHRONIC INFECTION	Adults, 5 to 10 percent; children, 25 to 50 percent; infants 90 percent	None	As a coinfection: low (< 5 percent) As a superinfection: high (70 to 95 percent)	None	High (≥ 85 percent)	Despite persistent viremia, unclear whether this virus causes chronic hepatitis
AVAILABLE IMMUNOPROPHYLAXIS	Vaccine and immune globulin	Vaccine and immune globulin	Hepatitis B vaccine and immune globulin prevent hepatitis B/hepatitis D coinfections only	None	None	None
LIKELIHOOD OF DENTAL WORKERS' OCCUPATIONAL EXPOSURE	Yes	No	Yes	No	Yes	Unknown
IMMUNIZATION RECOMMENDED FOR DENTAL PERSONNEL	Yes	No	Yes	No	None available	No
U.S. POPULATIONS WITH HIGHEST ATTACK RATES	Young adults aged 25 to 39 years	Children aged 5 to 14 years	Hemophiliacs, injecting drug users, people who have received multiple blood transfusions	People aged 15 to 40 years [‡]	Young adults (aged 20-39 years) with high-risk behaviors	Hemophiliacs, injecting drug users, people who have received multiple blood transfusions
TREATMENT OF CHRONIC HEPATITIS [§]	Interferon- α	Not applicable	Interferon- α	Not applicable	Interferon- α ; combination therapy with interferon and ribavirin	None
PERCENTAGE OF SUSTAINED RESPONSES AMONG PATIENTS TO INTERFERON- α THERAPY	33 percent respond to treatment overall; 8 percent clear surface antigen (HBsAg)	Not applicable	15 to 25 percent respond; = 17 percent clear HBsAg	Not applicable	20 to 30 percent	Evidence suggests that sustained responses seldom occur

* The complete epidemiology of hepatitis G has not been elucidated.
[†] Hepatitis delta, or D, was discovered in 1977 and was more fully characterized by the mid-1980s.
[‡] Hepatitis E is not endemic to the United States.
[§] Researchers are evaluating the effectiveness of combination antiviral therapy.

that combined therapies may be more effective than use of either agent alone.^{87,88} In December, the FDA approved Rebetron Combination Therapy (Schering-Plough Corp.), which consists of ribavirin (Rebetol, Schering-Plough Corp.) capsules and IFN- α 2b recombinant (Intron, Schering-Plough Corp.) injection for treatment of patients with chronic hepatitis C.⁸⁹

Reports in the literature relating to antiviral therapy suggest that although HGV is sensitive to interferon, only few patients exhibit a sustained response and only rarely do they clear HGV RNA. Once therapy ended, most patients who became HGV RNA-negative during therapy experienced a recurrence of HGV RNA over time.^{75,78,90} Ribavirin therapy appears to be ineffective.⁷⁵

Because the association among HGV, chronic hepatitis and liver disease is unknown, treatment targeting HGV is not currently recommended.⁷⁵

DISCUSSION

Advances in technology have led to identification and diagnosis of six types of viral hepatitis. (The table provides a summary of these.) There is little doubt that with continued advances, one or more hepatitis viruses will be identified in the near future. The epidemiology of five types of hepatitis is well-known. Vaccine and immune globulin are available and confer protection against three types. Four of the known viruses are bloodborne, and three of these—HBV, HCV and HDV—are of concern to dental practitioners.

In the United States, approximately 153,000 active dentists, 100,000 active dental hygienists and 200,000 active dental assis-

tants work in an environment where exposure to blood, blood spatter and aerosolization of saliva contaminated with blood can occur continually.⁹¹ HBV, HCV and HDV are bloodborne viruses that can be transmitted in the dental office by percutaneous exposures and potentially through mucosal exposures. These particular viruses are problematic because they can produce acute or chronic hepatitis. HBV is much easier to contract or transmit than HCV. However, immune globulin and vaccines are effective in providing long-term protection against HBV and HDV, whereas no immunoprophylaxis is available for preventing HCV. An alarmingly large proportion of people who have acute HCV infection develop chronic infection and chronic liver disease.

Adherence to infection control measures—as described in two Occupational Safety and Health Administration publications, the bloodborne pathogens standard (29 CFR 1910.1030, published in 1991)⁹² and “Controlling Occupational Exposure to Bloodborne Pathogens in Dentistry” (published in 1992)⁹³; in CDC’s “Recommended Infection-Control Practices for Dentistry” (published in 1993)⁹⁴; and in the American Dental Association’s “Infection Control Recommendations for the Dental Office and the Dental Laboratory” (published in 1996)⁹⁵—will reduce the risk of occupational transmission of bloodborne pathogens while alleviating dentists’ fears about treating patients with viral hepatitis. The taking of thorough health histories; use of personal protective equipment; proper hand-washing technique; implemen-

tation of engineering and work practice controls; careful handling and disposal of sharp instruments; sterilization of instruments; disinfection of dental units and environmental surfaces; immunization against hepatitis B; and compliance with current postexposure protocols as recommended by ACIP all are sound infection control practices and undoubtedly have already saved countless lives of dental personnel.^{15,71,92-95}

Fortunately, the occupation of dentistry does not place dental personnel at higher risk of acquiring hepatitis A than the general U.S. population, and therefore it is not recommended that dental HCWs receive the hepatitis A vaccine. Nevertheless, dental HCWs who plan to travel to developing countries for vacation or to practice dentistry should receive the HAV vaccine or immune globulin because of exposure due to location (rather than to occupation). Although HEV poses no threat to dental HCWs practicing in the United States, it is a threat to people traveling or working in developing countries because of unsafe drinking water supplies. Unfortunately, no vaccine or immune globulin is available to prevent HEV infection. Pregnant women, especially, should be advised of the risks of traveling to HEV-endemic areas because of high case fatality rates associated with HEV infection.

CONCLUSION

Dentists should avail themselves of the latest information on viral hepatitis and disseminate that information to the members of their staffs. As required by OSHA, dental personnel at risk of exposure must be

offered the hepatitis B vaccine within 10 working days of initial assignments of employment.⁹² They should be informed that this vaccine also will protect them against HBV-HDV coinfections, but not against HBV-HDV superinfections if they already are chronically infected with hepatitis B. The latest CDC recommendations regarding practice restrictions for HCWs infected with HBV were published in 1991 under the title "Recommendations for Preventing Transmission of Human Immunodeficiency Virus and Hepatitis B Virus to Patients During Exposure-Prone Invasive Procedures."⁹⁶ No CDC recommendations exist regarding practice restrictions of HCWs infected with hepatitis C.²⁸ Future recommendations may be made if additional evidence on risk of transmission from HCW to patient warrants them.

The ADA has prepared "Resource Manual for Support of Dentists With HBV, HIV, TB and Other Infectious Diseases," a guide that explores some of the legal issues surrounding providers infected with the aforementioned diseases.⁹⁷ Infected practitioners should be cognizant of federal and state laws that afford them protections, as well as of the laws that may restrict their practice of dentistry. Dental HCWs should strictly adhere to infection control policies because they are effective in preventing transmission of all bloodborne pathogens, including hepatitis viruses. ■

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