LEARNING OBJECTIVES

After completion of this chapter individuals should be able to:

1. Define hepatitis and its symptomatology.
2. Distinguish between the various viruses associated with hepatitis.
3. Describe the general features of hepatitis A, hepatitis B, hepatitis C, hepatitis D, and hepatitis E, including the etiology, transmission, diagnosis, sequelae, and prophylaxis.
4. List and discuss the serologic markers used in the diagnosis of various forms of viral hepatitis.
5. Describe the implications of the carrier states for hepatitis B and hepatitis C.
6. List the risk factors associated with the different hepatitis viruses.
7. Comprehend the occupational considerations for viral hepatitis and transmission risks for healthcare workers.
8. Understand the chemotherapeutic approaches for management of persons infected with hepatitis viruses.
9. Describe the types and efficacy of available hepatitis A and hepatitis B vaccines.
INTRODUCTION

Two diseases have been primary occupational concerns over the past few decades for healthcare personnel (HCP): viral hepatitis and acquired immune deficiency syndrome (AIDS). Prior to the late 1970s, many dentists, hygienists, assistants, and dental lab technicians learned about viral hepatitis in school, but because there were only limited epidemiological studies and little infection control data available, people generally accepted the risk with little worry. Unfortunately, several dental professionals were infected, with some subsequently manifesting disease sequelae ranging from development of an infectious carrier state to cirrhosis, hepatocellular carcinoma, and even death. Viral hepatitis can have a short- or long-term incubation interval, depending on the etiologic agent involved. The possibility of prolonged symptomatic and asymptomatic sequelae to primary infection also exists. Fortunately, as much more is understood regarding modes of transmission, diagnosis, and prevention, approaches about viral etiologies, sensitive assays have been developed and effective vaccines have been produced against most of the major viral etiologies. This chapter examines the challenge that viral hepatitis continues to pose for the dental profession and places this challenge in proper perspective.

VIRAL HEPATITIS: THE MAJOR BLOODBORNE CHALLENGE

Hepatitis, or inflammation of the liver, can be caused by several viruses and a variety of other nonmicrobial etiologies. It can be caused by various disease states and drug reactions. It is therefore important for dental healthcare personnel (DHCP) to remember at the outset that a patient history of hepatitis does not automatically signify a case of viral hepatitis. While several different viruses can induce hepatic symptoms and abnormalities, currently at least seven distinct viruses have been identified as major causes of viral hepatitis, with manifestations ranging from acute to chronic disease. Table 2-1 lists these and other viruses that can cause hepatitis. Currently, at least six viruses are believed to account for the overwhelming majority of viral hepatitis infections (Table 2-2). While there are additional hepatitis viruses which could be added here, the following will discuss the five most extensively studied, the infections they cause, and the occupational implications for health professionals.

Hepatitis conditions in general are classically divided into prodromal, icteric, and convalescent phases. During the prodromal stage, nonspecific respiratory and/or gastrointestinal symptoms can develop. These can include malaise, loss of appetite, headaches, nausea, and flu-like
respiratory symptoms. When present, fever is usually low-grade. With specific regard to hepatitis B, arthritis and maculopapular skin rashes develop just prior to definitive positive diagnostic assays indicating viral infection. Since many cases of hepatitis are subclinical, all or none of these manifestations may occur. The subsequent icteric phase is characterized by onset of jaundice and dark, foamy urine. Stool color changes also may occur during this period, where it may be seen as lightening to a grayish-white appearance. Symptomatology of the icteric phase is also variable. While jaundice detected either on the skin, sclera, nail beds, or gingiva is generally considered to be the hallmark hepatitis manifestation, the majority of infections may only result in elevation of certain enzymes associated with liver cells (aminotransferase; transaminases). Elevation of these biochemical markers in a person’s blood usually occurs a few days before or at the time of clinical symptoms. Other physical signs can include hepatic tenderness, hepatomegaly, and splenomegaly. These manifestations disappear during the convalescent or recovery phase of infection. However, even in those individuals who recover normally without any long-term, chronic sequelae, malaise and fatigue may persist for weeks to months. Different types of viral hepatitis may present with variations from the above generalized description.

HEPATITIS A

Hepatitis A (Table 2-3) is caused by the hepatitis A virus (HAV), a small, single-stranded 27-nm ribonucleic acid (RNA) agent that shares properties with members of the picornavirus family. HAV has been shown to exhibit features similar to the enteroviruses. It is more stable to temperature and pH changes than the enteroviruses, however, and is also able to survive in feces and exudates, and for weeks on inanimate surfaces. The virus was first described in 1973 and the disease was formerly known as “infectious hepatitis.” This term is no longer considered an appropriate description. The illness caused by HAV characteristically has an abrupt onset with fever, malaise, anorexia, nausea, abdominal discomfort, icterus, inflammation of the liver, and jaundice. In approximately 20% of cases, relapse in liver inflammation may be seen, with some cases lasting approximately 6 months. Severity of illness is related to age. In children, most infections are asymptomatic and illness usually is not accompanied by jaundice. However, most infected adults become symptomatically ill, with jaundice. Death among patients with reported cases is infrequent (occurring in approximately 0.6% of patients) and is related to infection occurring during older age. HAV infection is self-limiting and recovery provides lifelong protection against recurrent disease.

HAV infection is common in many developing countries. In these areas most infections may occur during childhood, often manifesting little or no symptomatology. Although this disease typically has a low mortality rate, the morbidity of hepatitis A infection worldwide was approximately 1.4 million new cases per year. The incidence of hepatitis A has decreased in the United States over the past few decades. In 1980, 29,087 new cases were reported in the U.S. with an estimated 234,000 new infections occurring in the population. This is contrasted with recent Centers for Disease Control and Prevention (CDC) figures for 2005, showing 4,488 new reported cases with an estimated 42,000 new cases. Although the incidence of hepatitis A has decreased in the U.S., it still accounts for over 30% of the reported acute hepatitis cases.
### TABLE 2-2 Comparison of Major Microbiological and Clinical Features of Viral Hepatitis

<table>
<thead>
<tr>
<th>Feature</th>
<th>Hepatitis A Virus (HAV)</th>
<th>Hepatitis B Virus (HBV)</th>
<th>Hepatitis C Virus (HCV)</th>
<th>Hepatitis D Virus (HDV)</th>
<th>Hepatitis E Virus (HEV)</th>
<th>Hepatitis G Virus (HGV)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Family characteristics</td>
<td>Picornaviridae; nonenveloped single-stranded RNA</td>
<td>Hepadnaviridae; double-stranded DNA</td>
<td>Flaviviridae; enveloped single-stranded RNA</td>
<td>Satellite; nonenveloped single-stranded RNA</td>
<td>Caliciviridae; RNA</td>
<td>Flaviviridae; RNA</td>
</tr>
<tr>
<td>Incubation period</td>
<td>15–40 days</td>
<td>50–180 days</td>
<td>30–150 days</td>
<td>21–90 days</td>
<td>15–70 days</td>
<td>unknown</td>
</tr>
<tr>
<td>Onset</td>
<td>Usually acute</td>
<td>Usually insidious</td>
<td>Usually insidious</td>
<td>Usually acute</td>
<td>Usually acute</td>
<td>Acute disease spectrum unknown</td>
</tr>
<tr>
<td>Prodrome: Arthritis/rash</td>
<td>Not present</td>
<td>Sometimes</td>
<td>Sometimes</td>
<td>Unknown</td>
<td>Not present</td>
<td>unknown</td>
</tr>
<tr>
<td>Transmission</td>
<td>Fecal-oral; poor sanitation</td>
<td>Parenteral; sexual contact; perinatal; other secretions (i.e., saliva)</td>
<td>Usually parenteral; sexual contact less common; perinatal</td>
<td>Usually parenteral; sexual contact less common</td>
<td>Fecal-oral; waterborne (common in developing countries)</td>
<td>Parenteral; perinatal frequent coinfection with HCV</td>
</tr>
<tr>
<td>Carrier state</td>
<td>No</td>
<td>Yes (5% to 10%)</td>
<td>Yes (&gt;85%)</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Possible manifestations</td>
<td>None reported</td>
<td>Hepatocellular carcinoma; cirrhosis</td>
<td>Hepatocellular carcinoma; cirrhosis</td>
<td>Hepatocellular carcinoma; cirrhosis</td>
<td>None reported</td>
<td>None reported</td>
</tr>
<tr>
<td>Mortality</td>
<td>0.1% to 0.2%</td>
<td>1% to 2%; higher in adults &gt;40 yrs</td>
<td>1% to 2%</td>
<td>2% to 20%</td>
<td>1% to 2% in general population; 20% in pregnant women</td>
<td>unknown</td>
</tr>
<tr>
<td>Homologous immunity</td>
<td>Anti-HAV</td>
<td>Anti-HBsAg</td>
<td>Not defined</td>
<td>Anti-HBsAg</td>
<td>Anti-HEV</td>
<td>Anti-HGV</td>
</tr>
</tbody>
</table>

Transmission of HAV occurs primarily by person-to-person contact, generally through fecal-oral contamination. HAV is shed in the feces of persons with viral infection, with spread of the virus commonly occurring by a person putting something in their mouth which has been contaminated with feces from an HAV-infected individual. Transmission can thus occur by direct person-to-person contact, poor sanitation, and intimate (intrahousehold or sexual) contact. Among the risk factors are daycare center contact, international travel, intravenous drug use, men who have sex with men, and persons with chronic liver disease. Indirect transmission of HAV via contaminated water or food is common, most often from raw or inadequately cooked shellfish. Sharing utensils, sharing cigarettes, and kissing are not believed to transmit the infection. It must be noted that approximately 45% of the U.S. cases of hepatitis A for 2005 did not relate any known risk factors. While DHCP do not typically have occupational exposure to HAV, appropriate attention to hand hygiene procedures and personal hygiene are some of the factors DHCP should be aware of in their overall infection control practices.

The incubation period of hepatitis A is 15–40 days (average 28–30 days). Sudden onset of illness is characteristic of hepatitis A, with the clinical course of infection ranging from asymptomatic to severe. High concentrations of HAV are found in stools of infected people. Fecal virus excretion reaches its highest concentration late in the incubation period and early in the prodromal phase of illness; it diminishes rapidly once jaundice appears. Fever is often present during acute illness, but symptoms may only last 2–7 days. A person’s greatest infectivity potential occurs during the 2-week period immediately before the onset of jaundice. Onset of symptoms is rapidly followed by a decrease in both viremia and infectiousness of the host. The virus has not been found in urine or other body fluids. Fortunately, a carrier state has not been demonstrated, nor has HAV been shown to induce chronic hepatitis. Instead, the virus is maintained in the population by serial propagation through human infection.

A reliable marker for immunity or even ongoing infection is the presence of anti-HAV in the serum. The diagnosis of acute hepatitis A is confirmed by finding anti-HAV of the immunoglobulin M (IgM) class in serum collected during the acute or early convalescent phase of disease. The antibodies persist for 4 to 6 weeks and are then replaced by high concentrations of IgG antibodies. These protective immunoglobulins appear in the convalescent phase of disease and remain detectable in serum thereafter, conferring lifelong protection against disease (Fig. 2-1). Commercial tests are available to detect IgM anti-HAV and total anti-HAV in serum.

**Hepatitis A Vaccines**

HAV has been grown successfully in culture and its genome has been cloned. A vaccine against hepatitis was developed and is being used in many countries. The rationale for development and use of a hepatitis A vaccine is the economic loss from prolonged convalescence associated with the infection. Development of HAV

<table>
<thead>
<tr>
<th>TABLE 2-3 Hepatitis A Virus Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Picornavirus (RNA)</td>
</tr>
<tr>
<td>2. Humans are only natural host</td>
</tr>
<tr>
<td>3. Depending on conditions, can be stable in environment for months</td>
</tr>
<tr>
<td>4. Virus can remain stable and infectious at low pH and moderate temperatures</td>
</tr>
<tr>
<td>5. Inactivated by high temperatures, formalin, and chlorine</td>
</tr>
</tbody>
</table>

**FIGURE 2-1** Hepatitis A serology. (From Serodiagnostic Assessment of Acute Viral Hepatitis. Abbott Laboratories, Diagnostic Division; North Chicago, IL; with permission.)
vaccines uses procedures designed to accomplish inactivation of the whole virus. Merck, Sharp & Dohme Research Laboratories was the first to release a hepatitis A vaccine, called VAQTA, which contains no detectable impurities and is free of residual formalin (which is used to inactivate the virus). This vaccine is very immunogenic and shows seroconversion in >95% of adults who receive one vaccine dose and approximately 100% of those who receive two doses. Children older than 12 months of age and adolescents demonstrate similar response rates (>97% after one dose and approximately 100% after two doses). Smith Kline Beecham also developed a formalin-inactivated vaccine, Havrix, which became available in 1995. Vaccination of groups of people known to be at high risk for HAV infection (i.e., travelers to HAV endemic countries, children in areas with high rates of hepatitis A, men who have sex with men, parenteral drug abusers, and recipients of clotting factors) has substantially reduced the disease burden. In addition, most cases of hepatitis A in the U.S. occur as community-wide outbreaks. Thus, prevention of disease became a priority for widespread vaccination of children and adults. In 2001 a combination vaccine (Twinrix) became available to protect against both hepatitis A and hepatitis B.

In 1999 the CDC’s Advisory Committee for Immunization Practices recommended that children living in states, counties, or communities with reported annual hepatitis A rates of 20 per 100,000 or higher between 1987 and 1997 be routinely vaccinated beginning at 2 years of age or older. Consideration of vaccination was also included for all children living in areas with reported hepatitis A rates of between 10 and 20 cases per 100,000 population. The most recent public health recommendations for hepatitis A vaccination published in 2006 are summarized as follows:

1. All children should receive hepatitis A vaccine at 12–23 months of age.
2. Vaccination should be integrated into the routine childhood vaccination schedule.
3. Children who are not vaccinated by 2 years of age can be vaccinated at subsequent visits.

HEPATITIS B

Hepatitis B virus (HBV) infection is a major worldwide cause of acute and chronic hepatitis, cirrhosis, and primary hepatocellular carcinoma. The virus first was described in 1965. The frequency of HBV infection and patterns of transmission vary significantly in different parts of the world. In the United States, Canada, Western Europe, New Zealand, and Australia it is a disease of low endemicity, with only a 0.1% to 2.0% incidence, in contrast to areas which demonstrate a 10% to 20% seroprevalence (Southeast Asia, China, and subSaharan Africa). Hepatitis B is most frequently acquired perinatally in the high prevalence regions, from infected mother to offspring, with a subsequent 90% risk of chronic HBV infection developing in those infants.

Globally, approximately 2 billion people have been infected, with estimates ranging from 350 to 400 million people being chronic carriers of the virus. Approximately 90% of the carriers live in less developed countries. HBV is the most frequent cause of chronic hepatitis in the world. This virus is also associated with as many as 80% of the cases of primary liver cancer with 1–1.5 million deaths each year attributable to hepatitis B sequelae. As a result this disease continues to be a leading cause of global infection and death. In the 1980s approximately 260,000 people were infected with HBV in the United States. Since the introduction of the hepatitis B vaccine and improved infection control precautions the estimated number declined to about 78,000 in 2001 and 51,000 for 2005. However, it is estimated that there are still approximately 1 million hepatitis B carriers in the United States of whom 20% to 40% will develop life threatening complications.

HBV Properties and Morphological Components

HBV infection is caused by HBV, a 42-nm, double-shelled DNA virus (Fig. 2-2, Table 2-4). The complete HBV virion is called the Dane particle. This particle is capable of replication and is the infectious agent. Several well-defined antigen–antibody systems have been associated with HBV infection. Hepatitis B surface antigen (HBsAg), formerly called “Australia antigen” or “hepatitis-associated antigen,” is found on the surface of the virus and on accompanying 22-nm spherical and tubular forms. These particles represent excess HBsAg produced during viral replication. They also compose the major proportion of detectable HBsAg following HBV infection. HBsAg remains the major diagnostic antigen for viral infection. The various subtypes (adr, adw, ayw, ayr) of
TABLE 2-4 Hepatitis Terminology

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Term</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>HAV</td>
<td>Hepatitis A virus</td>
<td>Etiologic agent of “infectious” hepatitis</td>
</tr>
<tr>
<td>Anti-HAV</td>
<td>Antibody to HAV virus</td>
<td>Detectable at onset of symptoms; lifetime persistence</td>
</tr>
<tr>
<td>IgM anti-HAV</td>
<td>IgM class antibody to HAV virus</td>
<td>Indicates recent infection with hepatitis A; tests positive up to 4–6 months after infection</td>
</tr>
<tr>
<td>HBV</td>
<td>Hepatitis B virus</td>
<td>Etiologic agent of “serum” or “long incubation” hepatitis; also known as Dane particle</td>
</tr>
<tr>
<td>HBsAg</td>
<td>Hepatitis B surface antigen</td>
<td>Surface antigen(s) of HBV detectable in large quantity in serum; several subtypes</td>
</tr>
<tr>
<td>HBeAg</td>
<td>Hepatitis Be antigen</td>
<td>Soluble antigen; antigen correlates with HBV replication, higher titer HBV in serum, and infectivity of serum</td>
</tr>
<tr>
<td>HBeAg</td>
<td>Hepatitis B core antigen</td>
<td>No commercial test available</td>
</tr>
<tr>
<td>Anti-HBs</td>
<td>Antibody to HBsAg</td>
<td>Indicates past infection with, and immunity to, HBV, passive antibody from HBIG, or immune response from hepatitis B vaccine</td>
</tr>
<tr>
<td>Anti-HBe</td>
<td>Antibody to HBeAg</td>
<td>Presence in serum of HBsAg carrier suggests lower titer of HBV</td>
</tr>
<tr>
<td>Anti-HBc</td>
<td>Antibody to HBcAg</td>
<td>Indicates past infection with HBV at some undefined time</td>
</tr>
<tr>
<td>IgM Anti-HBc</td>
<td>IgM class antibody to HBcAg</td>
<td>Indicates recent infection with HBV; tests positive for 4–6 months after infection</td>
</tr>
<tr>
<td>HCV</td>
<td>Hepatitis C virus</td>
<td>Name for one virus associated with PT-NANB</td>
</tr>
<tr>
<td>Anti-HCV</td>
<td>Antibody to Hepatitis C virus</td>
<td>Marker of previous HCV infection; does not specifically indicate immunity or viral carrier state</td>
</tr>
<tr>
<td>HEV</td>
<td>Hepatitis E virus</td>
<td>Proposed name for ET-NANB</td>
</tr>
<tr>
<td>HDV</td>
<td>Delta virus</td>
<td>Etiologic agent of delta hepatitis; only causes infection in presence of HBV</td>
</tr>
<tr>
<td>HDAG</td>
<td>Delta antigen</td>
<td>Detectable in early acute delta infection</td>
</tr>
<tr>
<td>Anti-HDV</td>
<td>Antibody to delta antigen</td>
<td>Indicates past or present infection with delta virus</td>
</tr>
<tr>
<td>IgG</td>
<td>Immune globulin (previously ISG, immune serum globulin, or gamma globulin)</td>
<td>Contains antibodies to HAV; lower titer antibodies to HBV</td>
</tr>
<tr>
<td>HBIG</td>
<td>Hepatitis B immune globulin</td>
<td>Contains high titer antibodies to HBV</td>
</tr>
</tbody>
</table>

HBsAg provide useful epidemiologic markers. Antibody against HBsAg (anti-HBs) develops during recovery from infection and is responsible for long-term immunity. Antibody to the core antigen (anti-HBc) is produced against an internal component of the virus. This serologic marker is present in all HBV infections and persists indefinitely. IgM anti-HBc appears early in infection and persists for 6 or more months; it is a reliable marker of acute or recent HBV infection. The hepatitis Be antigen (HBeAg) is a third antigen, the presence of which correlates with HBV replication and high infectivity. Antibody to HBeAg (anti-HBe) develops in most HBV infections and correlates with lower infectiousness of the patient.

Figure 2-3 shows the typical serologic pattern of an acute HBV infection with subsequent recovery and immunity. This information is presented along interpretations of other HBV serologic profiles regarding immunity and carrier status in Table 2-5.

Onset of hepatitis B is generally insidious with clinical manifestations observed to vary for both acute and chronic infection. The incubation period of HBV is long: 50 to 180 days (average 60 to 120 days). This disease has a variety of ultimate outcomes including a carrier state, cirrhosis, acute hepatitis, and primary liver cancer (Fig. 2-4). Clinical symptoms and signs in acute cases include combinations of anorexia, malaise, nausea, vomiting,
abdominal pain, and jaundice. Skin rashes, arthralgia, and arthritis also can occur. Several of these constitutional symptoms can precede the hallmark manifestation of jaundice by 1–2 weeks. Overall mortality rates for reported cases generally do not exceed 2%. In some instances these fatalities occur as a result of fulminant hepatitis which can progress rapidly.

Chronic hepatitis B is defined by the presence of HBsAg and persistence of HBV infection for at least 6 months. While viral chronic carriers can develop disease specific symptoms of cirrhosis or hepatocellular carcinoma, many may present with severe fatigue, nausea, anorexia, and upper right quadrant tenderness. This chronic persistence of HBV infection develops in about 5% to 10% of adolescents and adults, which presents a significant occupational risk for nonimmune health professionals. The risks are even greater when an HBV chronically infected woman transfers the infection to newborn via the perinatal route. There can be as high as an 80% to 90% risk of infection for the newborn, of which 90% of those children will become chronic HBV carriers themselves. This condition greatly increases their risk for cirrhosis or hepatocellular carcinoma as they age.

Modes of Transmission

HBV is capable of being transmitted parenterally, sexually, and vertically. The parenteral mode includes percutaneous and nonpercutaneous routes, both of which have significance in dentistry. Dental treatment involves the use of many small, sharp instruments which provide multiple opportunities for inadvertent percutaneous wounds to the operator. Performance of dental hygiene procedures, handling impressions, dental casts, and also while gathering contaminated instruments and cleaning them to remove debris before sterilization also provide potential occupa-

<table>
<thead>
<tr>
<th>Tests</th>
<th>Results</th>
<th>Interpretation</th>
</tr>
</thead>
<tbody>
<tr>
<td>HBsAg</td>
<td>negative</td>
<td>susceptible</td>
</tr>
<tr>
<td>anti-HBc</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>anti-HBs</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>HBsAg</td>
<td>negative</td>
<td>immune because of natural infection</td>
</tr>
<tr>
<td>anti-HBc</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>anti-HBs</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>HBsAg</td>
<td>negative</td>
<td>immune because of hepatitis B vaccination</td>
</tr>
<tr>
<td>anti-HBc</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>anti-HBs</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>HBsAg</td>
<td>positive</td>
<td>acutely infected</td>
</tr>
<tr>
<td>anti-HBc</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>IgM anti-HBc</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>anti-HBs</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>HBsAg</td>
<td>positive</td>
<td>chronically infected</td>
</tr>
<tr>
<td>anti-HBc</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>IgM anti-HBc</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>anti-HBs</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>HBsAg</td>
<td>negative</td>
<td>four interpretations possible*</td>
</tr>
<tr>
<td>anti-HBc</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>anti-HBs</td>
<td>negative</td>
<td></td>
</tr>
</tbody>
</table>

* (a) may be recovering from acute HBV infection; (b) may be distantly immune and test not sensitive enough to detect very low level of anti-HBs in serum; (c) may be susceptible with a false positive anti-HBc; or (d) may be undetectable level of HBsAg present in the serum and the person is actually a carrier.

From Centers for Disease Control and Prevention.
patient. While rare, transmission via this latter route does occur and has been documented. The most recent incident involved patient-to-patient HBV transmission in an oral surgery practice. This case was the only proven instance of patient-to-patient transmission in a dental setting and the first documented HBV transmission to dental patients since 1987.

Vertical transmission is also possible, with HBV passed perinatally from infected pregnant carriers or acutely infected mothers to their children via intimate, nonsexual contact. It can be transmitted during delivery, labor, or, less frequently, the gestational period. Perinatal HBV infections have a high infectivity rate of 70% to 90% compared with 10% to 40% during infancy. Perinatal transmission also has a high rate of progression into a carrier state. There is also the potential of transmission of HBV at birth from a woman who has progressed to the carrier state by infection from sexual contact, her own occupational exposure, or personal risk behavior. The development of the carrier state in the newborn infant is then possible, with a resultant increase in that child’s ultimate risk for primary hepatocellular carcinoma later in life.

**Frequency of Infection**

Until the 1980s most dentists believed that there were few potential HBV carriers in their practice and, hence, that there was little chance of infection in their office or indeed in the profession as a whole. They were not alone because the majority of the medical profession, including staff members of most hospitals, believed the same myth. The number of patient population groups that have a significantly increased prevalence of HBV infection, and hence an increased prevalence of the carrier state, is much larger than one would imagine. Many individuals remain unaware of their HBV infection. While the term “risk group” previously had the unfortunate consequence of causing some clinicians to use special “extra” infection control precautions for certain types of patients, delineation of certain populations with increased HBV risks was important in targeting groups of persons for receipt of hepatitis B vaccination soon after availability of the vaccine in 1982. These included providers of healthcare, patients in hemodialysis and hematology/oncology units, clients and staff of institutions for developmentally disabled persons, newborns of hepatitis B carrier mothers, and ethnic populations with a high incidence of disease (i.e., native born Alaskans and Pacific islanders). Please note that the dentist and the entire clinical dental staff are included in these high-risk populations. Why is this so?

HBV is an insidious disease, but fortunately with the widespread administration of the hepatitis B vaccine since its availability in 1982, the incidence has declined substantially in the U.S. and many other countries. Prior to 1982 there were approximately 300,000 new annual cases and the number of chronic HBV carriers was thought to be as high as 750,000. With the adoption of universal vaccination programs, the number of estimated new cases dropped to 78,000 in 2001. This decline has continued and for 2006 an estimated 46,000 persons, primarily young adults, were infected. One-quarter became ill with jaundice with approximately 5,000 people developing chronic liver disease. The U.S. still has approximately 1,000,000 HBV-infected carriers. Of major concern here is the progression of disease whereby chronic
active hepatitis develops in approximately 25% of carriers, often leading to cirrhosis. HBV carriers also have a risk of primary liver cancer that is 12 to 300 times higher than that of other people. Most infections cause no symptoms or, at most, very nonspecific symptoms. This is because some of the symptoms of HBV are familiar to busy people: headache, mild gastrointestinal upset, general fatigue, and/or a few “stiff joints.” It is easy to attribute these symptoms to too much coffee, late hours, overworking, or a mild case of the flu. Jaundice, the one presenting sign most believed to be pathognomonic of hepatitis, is unfortunately not routinely present as most HBV cases are anicteric. Depending on the route of transmission, virulence of the inoculum, and host resistance factors, only half or less of infected persons actually show jaundice. In addition, development of jaundice usually follows the appearance of HBsAg and HBeAg in the blood. Therefore even when jaundice develops the patient already has been potentially transmitting the disease. Thus, the major challenge in dental practice regarding HBV is to stop transmission from patient to dental staff, dental staff to practitioner, practitioner to patient, patient-to-patient, and dental staff to close intimate contacts (family) by using appropriate infection control measures.

As many as 80% of all HBV infections are undiagnosed. Unless patients have a history of immunity to HBV either from recovery of viral infection or a positive response to vaccination, a patient’s medical history may therefore not be reliable. This realization serves as a basis for current standard infection control precautions—all patients must be regarded as potential HBV carriers and/or infected with other bloodborne pathogens. In this regard, the HBV carrier is central in the epidemiology of HBV transmission. A carrier is defined as a person who has HBsAg-positive serologic results on at least two occasions at least 6 months apart. In almost all instances anti-HBs is not detectable in viral carriers and, therefore, HBsAg titers in these patients remain positive. Figure 2-5 outlines the serologic profile of the carrier state in chronic hepatitis B. Although the likelihood of infectivity is best correlated with concentrations of HBeAg in blood, any person with positive results for HBsAg is potentially infectious. The likelihood of the carrier state developing varies inversely with the age at which infection occurs. During the perinatal period, HBV transmitted from HBeAg-positive mothers results in HBV carriage in as many as 90% of infected infants, whereas 6% to 10% of acutely infected adults become carriers. Unfortunately, the HBV carrier state develops more commonly with asymptomatic, subclinical HBV infection versus acute infection. Additionally, carriers with an asymptomatic, subclinical infection are more likely to be HBeAg positive, indicating that they are in a more infectious, contagious state and therefore are more liable to transmit the disease.

Prevalence of Infection in the Dental Profession

A historically important study that is often quoted as a resource for HBV occupational risks in the dental profession was performed in 1972 at the American Dental Association (ADA) annual session. At that time, 1,245 general practitioners were screened for HBsAg and anti-HBs. Of the dental students or dentists in private practice who were screened, 3.3% reported a positive hepatitis B history, whereas blood screening showed that 13.6% had positive serologic tests for previous HBV infection. More recent data from blood specimens collected at the 2005 ADA annual session indicated a decrease to 8.5% of dentists and 6.8% of dental hygienists demonstrating serum markers indicative of past or present hepatitis B infection. Six chronic hepatitis B carrier dentists (0.51%) and no hygienists or dental assistants were identified as HBV carriers during the 2005 ADA session. Although more dentists are becoming immunized against HBV via vaccine, this does not mean that the risk of infection for the nonimmune dental professional has decreased. Other studies in the mid-1980s focused on dental specialties and indicated that as many as 38.5% of oral surgeons had positive serologic results for HBV infection. When data from multiple reports were analyzed, results indicated that the general dentist had a three times greater risk of hepatitis exposure compared with the general U.S. population (Table 2-6). In addition, the risk of nonimmunized surgical specialists (i.e., oral surgeons) was approximately six times that of the general U.S. population.

Investigation assessing the presence of virus in oral fluids from known HBsAg carriers detected HBV in >70% of salivary samples collected from known carriers. The virus also has been transmitted by a human bite and can be detected in nasopharyngeal secretions and gingival
crevicular fluid. The greatest concentration of HBV detected intraorally is in the gingival sulcus. In many patients’ mouths this area is inflamed routinely, easily allowing blood to mix with saliva and thus making the fluid potentially infectious for HBV. Despite these observations, however, the risk of HBV infection is more a factor of exposure to blood than general patient contact.

HBV Carrier State and Dentistry

Table 2-7 lists studies demonstrating that some dentists have transmitted HBV infection to their patients. Most often these cases were investigated by the CDC on finding clusters of HBV infections and determining a common factor of dental care by a single dentist within the previous 2 to 6 months before illness. The most outstanding case involved a 46-year-old male dentist from Pennsylvania who had no history of hepatitis or any disease with comparable symptoms but transmitted the same subtype of hepatitis that he was found to have to 55 of his patients. He rarely wore gloves while performing dental procedures before the incident occurred. He did wear gloves during the subsequent investigation and only two additional cases of hepatitis developed in more than 4,300 patients seen. Barrier techniques (mask, gloves, protective eyewear) have been shown time and again to be effective in preventing HBV transmission. Additionally, in 1984, 26 cases of HBV infection were reported in a dentist’s practice in late 2001, public health investigators were unable to identify the specific mechanism of cross-infection. One possibility expressed was the thought that cross-contamination from an environmental source may have occurred. Even without the identification of the mode of HBV transfer, the rarity of such an event in dentistry attests to the overall success dentistry’s infection control practices. The fact that it did occur, however, is a reminder that the stakes are high in preventing cross-infection and the necessity for performing everyday cleaning. This most recent case reinforces the principle that, even though appropriate standard precautions are

As can be noted from looking at Table 2-7, no documented cases of HBV transmission to dental patients were found from 1987–2001. Unfortunately a report in the May 1, 2007, issue of the *Journal of Infectious Diseases* quickly returned hepatitis B to the forefront of dental attention and concern. Although the CDC was able to document that a rare case of patient-to-patient transmission of HBV had occurred in an oral surgery practice in late 2001, public health investigators were unable to identify the specific mechanism of cross-infection. One possibility expressed was the thought that cross-contamination from an environmental source may have occurred. Even without the identification of the mode of HBV transfer, the rarity of such an event in dentistry attests to the overall success dentistry’s infection control practices. The fact that it did occur, however, is a reminder that the stakes are high in preventing cross-infection and the necessity for performing everyday cleaning. This most recent case reinforces the principle that, even though appropriate standard precautions are

<table>
<thead>
<tr>
<th>Author and Year</th>
<th>No. of Patients</th>
<th>Practice</th>
</tr>
</thead>
<tbody>
<tr>
<td>Levin, Maddrey, Wands, and Mendeloff, 1974</td>
<td>13</td>
<td>General dentist</td>
</tr>
<tr>
<td>Williams, Panison, and Berquist, 1975</td>
<td>0</td>
<td>General dentist</td>
</tr>
<tr>
<td>Goodwin, Fannin, and McCracken, 1976</td>
<td>37</td>
<td>Oral surgeon</td>
</tr>
<tr>
<td>Watkins, 1976</td>
<td>15</td>
<td>Oral surgeon</td>
</tr>
<tr>
<td>Rimland, Parkin, Miller, and Schrank, 1977</td>
<td>55</td>
<td>Oral surgeon</td>
</tr>
<tr>
<td>Reingold, et al, 1982</td>
<td>12</td>
<td>Oral surgeon</td>
</tr>
<tr>
<td>Ahtone and Goodman, 1983</td>
<td>4</td>
<td>General dentist</td>
</tr>
<tr>
<td>Shaw, et al, 1986</td>
<td>26</td>
<td>General dentist</td>
</tr>
<tr>
<td>Centers for Disease Control, 1987</td>
<td>4</td>
<td>Oral surgeon</td>
</tr>
</tbody>
</table>
effective, they do not necessarily eliminate all risks. Despite what we would like to see as 100% protection, infection control precautions are not absolute. When all components are integrated into a total program, they function very well by minimizing and reducing the potential for cross-infection.

**PREVENTION OF TRANSMISSION VIA IMMUNOPROPHYLAXIS**

**Active and Passive Immunity**

Scientific and clinical evidence accumulated since the late 1970s strongly shows HBV transmission can be stopped in the dental office. Transmission can be prevented by neutralization of the host reservoir (eradication of all HBV sources), interruption of the modes of transmission (infection control practices), or immunization of susceptible hosts. Principles of immunization will be presented only briefly here, with further discussion included in Chapter 7. To understand immunoprophylaxis, one must understand active and passive immunization. Passive immunity occurs by transferring preformed antibodies from an actively immunized host to a person in need of immunity. The protection provided is transitory, onset is immediate, and examples are injection of immune serum globulin (ISG) or HBIG. In contrast, active immunity develops from stimulation of one’s own immune response. Protection is provided only after a latent period, but benefits for the immunized person can be well worth it, as long-term immunity can develop and be maintained.

ISG primarily provides protection against HAV infection and is relatively inexpensive. Passive immunoprophylaxis via HBIG provides protection against HBV infection for approximately 2 months and is expensive. Active preincident immunity is preferable. Active immunity can be conferred through host recovery from acute infection or subclinical disease or through hepatitis B vaccination.

**Hepatitis B Vaccines**

**Plasma-Derived Vaccine**

The groundwork for the success of an immunizing preparation was set by Krugman, et al, in a classic series of studies that found that a 1:10 dilution of hepatitis B infective serum (strain MS-2) lost infectivity but retained its antigenicity when boiled for 1 minute. When used as a vaccine, this preparation prevented or modified the course of HBV in approximately 70% of subjects who were challenged later with HBV. MS-2 serum contained large quantities of HBsAg. Subsequent vaccine work focused on the extraction and purification of this noninfectious, viral coat protein for use as the antigen preparation in development of a component vaccine. This effort was fostered by the observation that HBV replication in infected people was not as efficient as once thought because large amounts of excess HBsAg particles are synthesized and passed into the patient’s circulation. As one recovers from infection, antibodies to this antigen (anti-HBs) are produced by the host’s immune system and provide protection against a recurrent viral attack.

Accumulated evidence also indicated that these HBsAg forms are present in high concentrations in the circulation of carriers of HBV. Thus, carriers with high serum HBsAg titers were shown to provide a supply of viral antigen for vaccine production. This achievement was crucial to the overall effort because HBV could not be cultured in vitro. Clinical tests were started in 1975 for Heptavax-B, the original plasma-derived hepatitis B vaccine, and the vaccine was introduced in the U.S. in 1982. This vaccine was developed and manufactured by Merck Sharp & Dohme and represented a milestone in immunology as the first clinically available vaccine derived from human sources. Approximately 5.6 million people worldwide received the plasma-derived vaccine before it was discontinued in 1989. The vaccine is given in three separate intramuscular injections; the first two doses are administered 1 month apart and the third dose is given 6 months after the first dose. The immunogenicity potential of the vaccine is shown in Table 2-8. After the first dose, approximately 30% of normal, healthy, young adult vaccine recipients respond by the formation of antibodies. The response rate increases to 75% after the second dose, rising to a current response rate of 90% to 95% after the third dose. Most people assume erroneously that all vaccines have a 100% response rate; however, no vaccine produces absolute seroconversion in 100% of cases. Those who respond to the vaccine by the formation of protective levels of anti-HBs are completely protected against development of active HBV, asymptomatic HBV infection, and the carrier state.

**TABLE 2-8 Antibody Responses* to Hepatitis B Three-Injection Vaccine Series by Age Group and Dose**

<table>
<thead>
<tr>
<th>Dose</th>
<th>Infants †</th>
<th>Teens and Adults ‡</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16% to 40%</td>
<td>20% to 30%</td>
</tr>
<tr>
<td>2</td>
<td>80% to 95%</td>
<td>75% to 80%</td>
</tr>
<tr>
<td>3</td>
<td>98% to 100%</td>
<td>90% to 95%</td>
</tr>
</tbody>
</table>

*Anti-HBs antibody titer of 10 mIU/mL or higher.
†Preterm infants less than 2 kg have been shown to respond to vaccination less often.
‡Factors that may lower vaccine response rates are age >40 years, male gender, smoking, obesity, and immune deficiency.
The vaccine production process was designed to thoroughly ensure a safe product. The collected serum, taken from human HBV carriers, was exposed to two biophysical purification steps and three chemical inactivation steps (pepsin at pH 2, 8 M urea, and 1:4,000 formalin), which virtually left an entirely safe suspension of HBsAg. Continued clinical monitoring of vaccine recipients by the CDC through 1984 and current monitoring by the Food and Drug Administration (FDA) indicate that there is no increased incidence of any severe side effects associated with the hepatitis B vaccine.

**Recombinant DNA Vaccines**

Advances in vaccine development continued to provide clinically useful preparations and in July 1986 the first vaccine made using recombinant DNA technology was licensed. Recombivax-HB, also from Merck Sharp & Dohme, became available for general use in the U.S. for the prevention of HBV infection in January 1987. This newer vaccine provided an alternative to the plasma-derived vaccine.

The recombinant vaccine is produced in cultures of *Saccharomyces cerevisiae* (common baker’s yeast), into which a plasmid containing the gene for HBsAg has been inserted. HBsAg subsequently is harvested after lysis of cultured yeast cells. Purified HBsAg protein then undergoes sterile filtration and treatment with formalin before packaging. Administered vaccine is designed to contain 10 µg of HBsAg protein per milliliter, absorbed with 0.5 mg/mL of aluminum hydroxide (alum), with thimerosal as a preservative. Another recombinant DNA hepatitis B vaccine, Engerix-B, has been produced by SmithKline Biologicals in Belgium. The only stated contraindication for Recombivax-HB is for patients who are hypersensitive to yeast or any component of the vaccine.

At one time there was some concern about the possibility of the hepatitis B vaccine transmitting human immunodeficiency virus (HIV) infection. Several studies addressed this issue and supplied evidence confirming a lack of HIV transmission with this vaccine. The evidence concerns four significant areas:

1. Direct testing of the inactivation steps used in the vaccine-manufacturing process indicated that all three of the inactivation procedures (pepsin at pH 2, 8 M urea, and 0.1% formaldehyde) inactivated HIV. Thus, if HIV were in the vaccine plasma pool, it would be inactivated by the vaccine production process.
2. Studies were performed looking for HIV nucleic acid sequences in the vaccine itself, using an HIV probe. It was determined that the vaccine contained no AIDS virus–related amino acid sequences. All protein in the vaccine coded specifically for HBsAg.
3. The third approach attempted to detect seroconversion to anti-HIV in hepatitis B vaccine recipients. No seroconversion was detected in people who received vaccine manufactured from plasma pools that contained plasma of donors at high risk for HIV infection.
4. Monitoring of patients with AIDS reported to the CDC and FDA focused on epidemiologic evidence of an association between hepatitis B vaccine and AIDS. As of 1994, no relationship has been detected between receipt of hepatitis B vaccine and an increased incidence of HIV infection.

In addition, the incidence of AIDS for hepatitis B vaccine recipients in CDC vaccine trials among homosexually active men in Denver and San Francisco did not differ from that for men screened for possible participation in the trials who received no hepatitis B vaccine because they were found to be immune. These and other reported observations clearly demonstrated that vaccination with the plasma-derived HBV vaccine posed no risk for HBV or HIV infection.

**Pretesting**

The issue of whether to pretest a person for anti-HBs immunity has been discussed at length since introduction of the vaccines. Pretesting can be cost-effective in large groups where the proportion expected to be antibody positive is substantial because those who are already anti-HBs positive are immune to HBV infection and therefore do not need the vaccine. Studies to date have shown that only 6.7% of vaccine recipients in dentistry were already immune. Thus, pretesting is not cost-effective in the average dental office, although it may be offered to potential vaccine recipients in an immunization program in accordance with the 1991 Occupational Safety and Health Administration (OSHA) standard. Unfortunately, there can be a significant number of false-positive reports for anti-HBs, particularly in a pretesting situation.

**Post-testing**

People electing to perform post-vaccination testing for anti-HBs should be aware of potential difficulties in interpreting the results. Serologic testing within 6 months of completing the primary series will differentiate people who respond to vaccine from those who fail to respond; however, the results of testing performed more than 6 months after completion of the primary series are more difficult to interpret. Therefore, post-testing should be scheduled soon after the last inoculation, preferably within 1–2 months.

A vaccine recipient who has negative results for anti-HBs several years after vaccination can be a primary nonresponder who remains susceptible to HBV or a vaccine responder whose antibody levels have decreased below detectability yet he or she is still protected against clinical disease. Should one not have responded, a second course of three additional doses of vaccine usu-
ally is prescribed by physicians. These extra doses will cause seroconversion in approximately 50% to 70% of the “first series” nonresponders.

**Antibody Persistence and Booster Dose**

Ongoing studies have shown that immunological memory in persons who have responded to vaccination with >10 U/mL of anti-HBs lasts for at least 23 years, and probably much longer. People who had demonstrable anti-HBs when initially tested, yet lost detectable anti-HBs on a subsequent blood test, have demonstrated a secondary anamnestic response that was protective against clinical infection when challenged with HBV. According to the CDC, it is not necessary to be tested routinely for anti-HBs each year after vaccination. The antibody response to properly administered vaccine is excellent for adults and children with a normal immune status and protection lasts as mentioned above because of the anamnestic response.

**Site of Injection**

There was some concern about a suboptimal response to the hepatitis B vaccine when it was administered into the buttocks. Post-testing of vaccine recipients early after vaccine introduction showed low seroconversion rates, with some response rates as low as 50%. A thorough follow-up of shipping techniques, vaccine storage techniques, retention of vaccine potency, and review of vaccine lots failed to identify any specific cause. A breakthrough occurred when the same vaccine lot was distributed to a general hospital and a health department in a large Canadian city. The health department had 100% seroconversion, whereas the general hospital had a much lower rate. The only difference was that the vaccine was administered into the deltoid muscle at the health department and the hospital administered the vaccine into the buttocks. Additional backtracking of the other sites reporting suboptimal responses indicated differences in site of injection to be the reason for the seroconversion discrepancies.

**HEPATITIS C**

In 1989, hepatitis C virus (HCV) was discovered using recombinant DNA technology. Until then and beginning in 1975, hepatitis C was previously termed parenterally transmitted non-A, non-B (NANB) hepatitis primarily because as many cases of bloodborne post-transfusion hepatitis could not be attributed to HAV, HBV, or any other known microorganism by serological assays. HCV has several characteristics similar to those of HBV: occurring after blood transusions, parenteral drug use, and accidental sharps exposures. HCV is an RNA virus whose structure appears closely related to the general Flavivirus and Pestivirus. A major difference between structural properties of HCV compared with those of other known hepatitis viruses is that different HCV strains can demonstrate extensive variations in genetic sequencing. This property, also called “genetic diversity,” is related to HCV being able to mutate within a host during viral replication. As a result, several genotypes, or quasi-species, with significant differences in the RNA genome can be isolated within an infected individual. The ability of HCV to mutate and modify viral surface components is a major factor in the very high rate of chronic HCV infection.

Clinically, the features of HCV infection are variable as with other hepatitis viruses. Most (60% to 70%) individuals with acute HCV infection are asymptomatic or have nonspecific symptoms similar to hepatitis A and hepatitis B. Clinically, HCV infection often induces less hepatic inflammatory reactions and, thus, usually manifests milder symptoms. The incubation period ranges from 30–150 days. HCV RNA can be detected in the blood as soon as 1 week after initial exposure. Antibodies to HCV, or anti-HCV, can be detected within 3 months after onset of infection in approximately 90% of patients (Fig. 2-6). Unfortunately, more than 85% of hepatitis C cases progress to chronic HCV infection. Chronic HCV can take as long as 20 years to develop and progresses without signs or symptoms until patients have advanced liver disease. Almost 80% of chronic cases are stable with mild to moderate histologic disease. The other 20% eventually develop more serious sequelae such as cirrhosis and liver cancer. In the U.S., HCV is the leading cause of liver disease and may account for 8,000 to 13,000 deaths per year. In the U.S. approximately 3 to 4 million individuals are infected with HCV, with about 2.7 million being chronic carriers. This makes HCV the most common form of viral hepatitis today. The CDC estimates that the number of new cases of acute HCV infection in the U.S. has fallen from approximately 230,000 per year in the 1980s to its current level of about 20,000 cases per year.

The primary route of transmission of HCV is via the blood and although HCV traditionally had been considered a transfusion-associated disease, most reported cases have not been associated with a blood transfusion. In recent years less than 5% of the reported cases have been related to blood transfusions. Illegal intravenous drug use accounts for the majority (60%) of reported cases of acute HCV infections. In contrast to HBV transmission, sexual transmission of HCV appears less efficient. Perinatal and familial transmissions have also been documented. Studies have shown that HCV RNA is found in the saliva of approximately half the patients with chronic HCV, but the rate of transmission through saliva is low. HCP are at risk for exposure to patient blood and possible subsequent infection from bloodborne diseases including HCV. However, HCV does not appear to be transmitted efficiently through occupational exposures.
to blood. The most recent follow-up studies of HCP exposed to HCV-infected blood through accidental percutaneous injury have determined an average low incidence of 1.8% (range, 0% to 7%) with one study determining that transmission occurred only from hollow-bore needles compared with other sharps. Although these studies have not documented seroconversion associated with mucous membrane or nonintact skin exposure, at least two cases of HCV transmission from a blood splash to the conjunctiva and one case of simultaneous transmission of HCV and HIV after nonintact skin exposure have been reported. Data are limited on survival of HCV in the environment. Compared with HBV, the epidemiologic data for HCV suggest that environmental contamination with blood containing HCV is not a significant risk for transmission in healthcare settings, with the possible exception of the hemodialysis setting where HCV transmission related to environmental contamination and poor infection-control practices has been documented.

The majority of studies indicate the prevalence of HCV infection among dentists, surgeons, and hospital-based HCP has declined and is currently similar to that among the general population, approximately 1% to 2%. In a study that evaluated risk factors for infection, a history of unintentional needlesticks was the only occupational risk factor independently associated with HCV infection. Unfortunately, multiple published reports have described transmission from HCV-infected surgeons which apparently occurred during performance of invasive procedures with the overall risk for infection averaging 0.17%. There have not been any studies of the transmission from HCV-infected DHCP to patients reported and the risk for such transmission appears limited.

Presently, a vaccine is not available for HCV. This is primarily because there are six major genetic types, multiple subtypes, and HCV mutates frequently. Immunoglobulin and antiviral agents are not recommended for postexposure prophylaxis (PEP) after exposure to HCV-positive blood. In addition, no guidelines exist for administration of therapy during the acute phase of HCV infection. However, limited data indicate that antiviral therapy might be beneficial when started early in the course of HCV infection. When HCV infection is identified early, the person should be referred for medical management to a specialist knowledgeable in this area. Additional information about PEP after occupational exposure to HCV is presented in Chapter 15. Therefore, prevention of occupational transmission of HCV in healthcare settings continues to rely upon routine use of standard infection control precautions during patient care. This includes appropriate use of personal protective equipment (e.g., gloves, masks, protective eyewear), safe handling of sharp instruments to prevent occupational exposure to blood, and continued education of DHCP about the risk and prevention of blood-borne diseases.

**FIGURE 2-6** Acute hepatitis C virus infection. (From Stevens. Update, 3(2):2, 1989, with permission.)
PART I  
MICROBIOLOGICAL RATIONALE FOR PRACTICAL INFECTION CONTROL IN DENTISTRY

DELTA HEPATITIS

Hepatitis D virus (HDV) (Fig. 2-7), originally called the delta agent, was discovered in 1977 by Rizzetto and colleagues in Italy. Extensive investigations since that time have established the fact that delta hepatitis is unique and distinct from HBV, although HDV depends on HBV for clinical expression. HDV is defective in that it requires HBV as a helper virus for an outer protein coat (HBsAg), and thus for replication.

HDV infection is worldwide in distribution and occurs in two major epidemiologic patterns. Delta is endemic in Mediterranean countries such as southern Italy, the Middle East, and parts of Africa, as it is in parts of South America. Nonpercutaneous transmission of HBV and HDV is believed to occur primarily by intimate contact and transmucosal exchange of body fluids. In areas where HDV infection is nonendemic, including North America and Western Europe, HDV infection is confined to groups with frequent percutaneous exposures such as intravenous drug users and hemophiliacs. Current data indicates that HDV accounts for <5% of chronic hepatitis cases reported each year in the U.S. Earlier studies in the U.S. found HDV to be detectable in 24% of HBsAg-positive drug users and approximately 50% of HBsAg-positive hemophiliacs, although cases have been reported. Only limited information is available on the prevalence of HDV infection in DHCP.

Hepatitis relating to delta infection occurs in two primary modes. The first mode is simultaneous infection with HBV and HDV. When simultaneous infection occurs, the acute clinical course of hepatitis often is limited, with resolution of both HBV and delta infections, although fulminant hepatitis may develop. The second mode involves acute delta superinfection in HBsAg carriers. In this situation, the patient already has a high titer of circulating HBsAg. These patients are more likely to have a serious and possible acute fulminant form of hepatitis that more often leads to chronic HDV infection. Some of these patients will become carriers of HDV as well as HBsAg-positive. HDV has been associated with several hepatitis outbreaks in the U.S. The largest outbreak, in Worcester, Massachusetts, included a total of more than 700 cases, with more than 200 parenteral drug users, from 1983 to 1988. More than 65 of these people had positive results for prior infection with HDV. There were 14 deaths, with 11 of these people being delta positive. Four dentists and one physician were infected through this outbreak. One dentist died of fulminant hepatitis in 1986. Another dentist became an HBV carrier and infected at least four patients in his practice. Another outbreak of delta hepatitis occurred in Durham, North Carolina. Fortunately, this outbreak was limited in size; there were only 86 cases of hepatitis and at least 15% of these had markers for HDV infection.

Because all dental staff members are at an increased risk of HBV infection and of possibly becoming HBV carriers (unless immunized), members of the dental profession are at risk of simultaneous infection with HDV and HBV. Therefore, DHCP who are immune to HBV following hepatitis B vaccination or who have developed natural active immunity against HBV following viral infection are also protected against clinical exposure to HDV infection.

HEPATITIS E VIRUS

Hepatitis E is a viral infection caused by a single-stranded RNA calcivirus that is transmitted enterically via the fecal-oral route. This virus was first described in 1980 and is most frequently found in sporadic waterborne epidemics reported in developing countries. Most outbreaks have occurred in India, Asia, portions of Africa, and Mexico and none have been reported in Europe, the United States, and Australia. Current epidemiologic information indicates that the hepatitis E virus (HEV) is transmitted indirectly by ingestion of fecally contaminated water. The most prominent risks have been found for people who live or travel to an endemic area, those individuals having close personal contact with HEV-infected persons, and consumption of contaminated food or water representing the greatest risks. HEV is not considered a routine occupational infection for healthcare providers in particular because parenteral transmissons are, at most, very rare occurrences. In addition, at this time the U.S. is not considered to be endemic for HEV infection.

When viral infection is followed by symptomatic disease, onset is acute with an incubation period ranging from 15–70 days. Resultant signs and symptoms are similar to other viral hepatitis infections including loss of appetite, fatigue, nausea, abdominal pain, and fever. However, serologic tests are available to distinguish hepatitis E from other viral etiologies. Clinical manifestations are most frequently found in young to middle age adults. While most cases of HEV disease are self-limiting with no chronic state sequelae, pregnant women are at a much greater risk for developing fatal fulminant hepatitis. As many as 20% to 25% of pregnant women in the second or third trimester of pregnancy may develop this life-threatening condition and, unfortunately, the rea-
sons for this remain unknown. This is in sharp contrast to the 1% to 2% mortality rate noted for the general population. Treatment for infection is supportive and an effective vaccine is not available.

SUMMARY

Several hepatitis viruses present a serious threat to members of the dental team. HBV and HDV infection represent the most life-threatening of these diseases; however, HCV has the highest carrier rate after infection. With the widespread application of hepatitis B vaccination in health professions since 1982, the overwhelming majority of dental and medical healthcare professionals are now immunologically protected against HBV and HDV. Presently, a vaccine is not available for HCV. Fortunately HCV does not appear to be transmitted efficiently through occupational exposures to blood. While the risk of HCV transmission appears very low in healthcare settings, standard infection control precautions must be used routinely to minimize occupational exposure and transmission.

Review Questions

1. Common hepatitis virus infections include hepatitis A, hepatitis B, and hepatitis C. Which is the least life-threatening and most mild of these diseases?
   A. Hepatitis A
   B. Hepatitis B
   C. Hepatitis C

2. The hepatitis A virus has which primary portal of entry?
   A. respiratory
   B. oral-fecal
   C. skin
   D. genital
   E. blood

3. This type of hepatitis may be traced to contaminated food or water, especially inadequately cooked shellfish.
   A. Hepatitis A
   B. Hepatitis B
   C. Hepatitis C
   D. All of the above
   E. Both A and B only

4. Which of the following characteristics applies to hepatitis A virus (HAV)?
   A. Antibodies against HAV have been shown to confer long-term protective immunity.
   B. Viral infection has a greater risk for development of a carrier state than hepatitis B virus infection.
   C. Cross-reactive immunity against HAV develops from receipt of the hepatitis B vaccine.
   D. HAV is a major occupational bloodborne infection risk for dental professionals.

5. The presence of ________ in a patient’s serum is considered to represent recovery and immunologic protection from hepatitis B.
   A. Anti-HBc
   B. Anti-HBs
   C. HBeAg
   D. Anti-HAV
   E. None of the above

6. The presence of anti-HBc in a person’s serum would indicate:
   A. the person is immune from reinfection with HBV.
   B. the person is a carrier of HBV.
   C. the person has been infected with HBV.
   D. the person has been vaccinated against HBV.
   E. the person is about to become jaundiced.

7. The greatest occupational healthcare worker risk for bloodborne infection is:
   A. hepatitis C virus.
   B. human immunodeficiency virus.
   C. hepatitis B virus.
   D. tuberculosis.

8. Which of the following have been involved in the transmission of hepatitis C?
   A. accidental needlesticks
   B. blood transfusions
   C. drug addicts sharing contaminated syringes
   D. all of the above

9. Which of the following statements is MOST appropriate for hepatitis D virus infection?
   A. common following ingestion of contaminated shellfish
   B. most common form of viral hepatitis from blood transfusion
   C. occurs as co-infection with HCV
   D. vaccine-preventable disease
   E. not involved in development of a carrier state

10. Artificial active immunization against HAV involves clinical use of a/an ________ vaccine, while the HBV vaccine is comprised of a/an ________.
    A. product/attenuated vaccine
    B. attenuated/product
    C. component/inactivated virus
    D. component/product
    E. inactivated virus/component
Critical Thinking

1. Using epidemiologic information, explain why hepatitis B virus is the bloodborne pathogen target for standard precautions.

2. You receive a copy of a patient’s hepatitis B serological profile. It reads: HBsAg negative, anti-HBc positive, and anti-HBs positive. What is your opinion about the patient’s possible history of hepatitis and immunity?

SELECTED READINGS


