

Hepatitis: What Every Healthcare Worker Needs to Know

1011 - 4 credits

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INTRODUCTION

The risk of cross-infection between dental practitioners, auxiliaries and patients is considered significant, particularly because most human microbial pathogens have been isolated from the oral cavity. It follows that the incidence of certain infectious diseases is significantly higher among dental professionals than that observed in the general population. Concern over these occupational disease states, with particular attention given to viral hepatitis, has led to increased awareness and understanding by health personnel in the matter of infectious disease and infection control. Health professional

organizations have issued guidelines and recommendations to assist treatment providers in the prevention of disease transmission. We consider the five major types of viral hepatitis in terms of clinical and asymptomatic disease, transmission and diagnostic tests, with major emphasis on hepatitis B and hepatitis C. The significance of infection to dental health care workers is discussed by considering manifestations of disease, chronic sequelae of infection, implications of a carrier state, clinical vaccines, and recommendations for appropriate infection control precautions.

COURSE OBJECTIVES

Upon completion of this course, the dental professional should be able to:

- Define hepatitis and its symptomatology.
- Distinguish between the various viruses associated with hepatitis.
- Describe the general features of hepatitis A, hepatitis B, hepatitis C, hepatitis D, hepatitis E, and hepatitis Non A-E including the etiology, transmission, diagnosis, sequelae, prophylaxis, and precautions for each.
- List and discuss the serologic markers that are utilized in the diagnosis of hepatitis B
- Identify risk factors for hepatitis B virus and other hepatitis viruses.
- Discuss the typical course of acute hepatitis B infection, from the prodromal state to recovery.
- Explain the carrier state for hepatitis B.
- Recall viral hepatitis contraction and transmission risks for dental health professionals.
- Describe the formulation and clinical applications of immune serum globulin, hepatitis B immune globulin, and available hepatitis B vaccines.
- Summarize the recommended standard precautions for infection control to be observed by dental professionals when treating patients.

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GLOSSARY

acute — short term and/or severe

adjuvant — one drug added to another to enhance the effectiveness

anicteric — not associated with jaundice
antibody — a specific protein produced by the immune system as a reaction to the presence of antigen
antigen — any substance which is capable, under appropriate conditions, of inducing a specific immune response and of reacting with the products of that response
asymptomatic — the absence of symptoms
bilirubin — a reddish-yellow organic compound derived from hemoglobin during normal and pathological destruction of erythrocytes
carrier — an individual harboring a disease agent, who may transmit the infection, without demonstrating apparent symptoms
chronic — of long duration, may or may not be severe
cirrhosis — chronic liver disease characterized by progressive destruction and regeneration of liver cells and increased connective tissue formation
etiology — the cause of a disease
fibrosis — formation of tissue composed of or containing fibers
fulminant — occurring suddenly, rapidly, and with great intensity, high mortality rate
gamma globulin — generally any serum protein exhibiting antibody activity
hemodialysis — the removal of certain elements of the blood by virtue of the difference in the rates of their diffusion through a semipermeable membrane
hepatitis — inflammation of the liver
icteric — relating to or marked by jaundice
inflammation — a fundamental pathologic process which occurs following any injury to tissue, such as that following the establishment and multiplication of microorganisms
in vitro — studies performed under artificial conditions
in vivo — in the living body or organism
jaundice — a yellowish staining of the skin, mucous membranes, and sclera with bilirubin and other bile pigments
malaise — a vague feeling of general body discomfort and uneasiness
necrosis — the sum of the morphological changes indicative of cell death and caused by the progressive degradative action of enzymes
parenteral — not through the alimentary canal but rather by injection through some other route
percutaneous — performed through the skin
prodromal — indicating the initial stage of a disease
recombinant vaccine — suspension of attenuated or killed microorganisms administered for the prevention of disease

sequelae — a condition following as a consequence of another disease

subclinical infection — a state in which the individual either does not experience all of the characteristic symptoms of a particular disease, or the manifestations are less severe

viremia — the presence of viruses in the blood

virion — a complete virus particle

OVERVIEW OF OCCUPATIONAL DISEASES OF DENTAL MEDICINE

When one considers the types of infections that are of major concern to dental professionals, it becomes readily apparent that a variety of bacterial, viral and other microbial agents are associated with many acute and chronic conditions. One group of these disease states, 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. The variability of these features has made it difficult to trace accurately the sources of suspected hepatitis outbreaks; however, as knowledge has increased about the viral etiologies and sensitive diagnostic assays have been developed, we have been able to find more answers to clinically important questions.

HEPATITIS

Definition and Symptomatology

The simplest definition of hepatitis is that the condition represents an inflammation of the liver. This does not differentiate between hepatitis induced by chemical agents or as a sequela to viral infection. It is thus of initial importance for dental professionals to remember that a patient history of hepatitis does not automatically signify viral hepatitis. This may be difficult to comprehend initially, because hepatitis conditions in general are similarly divided into prodromal, icteric and convalescent phases, regardless of the etiologic agents.

During the initial prodromal stage, non-specific respiratory and/or gastrointestinal symptoms can arise. Patients may complain of a variety of symptoms, including malaise, loss of appetite, headaches, nausea and flu-like respiratory symptoms. Fever may be present but is usually low-grade. Just before the definitive diagnosis of hepatitis B, for example, a highly suggestive prodromal series of symptoms can become manifest: arthritis and widespread maculopapular skin rashes. It is important to note that all or none of these manifestations may occur, as many cases

of hepatitis are subclinical and therefore asymptomatic.

The subsequent icteric phase is characterized by the appearance of jaundice and dark, often foamy urine. Of the two, darkened urine is generally noted most frequently by patients. A change in stool color also may occur during this period, in some instances lightening to a grayish-white appearance. Symptomatology in the icteric phase is also variable, as evidenced by retrospective studies in which diagnosed patients were asked to recall earlier symptoms. While the clinical sign of jaundice detected either on the skin, sclera, nail beds, or gingiva is generally regarded as the hallmark manifestation of hepatitis, the majority of infections may only result in elevation of certain serum enzymes associated with liver cells (aminotransferase; transaminases). Elevation of these biochemical markers in blood usually occurs a few days prior to or at the time of clinical symptoms. Other physical signs of hepatitis include hepatic tenderness, hepatomegaly and splenomegaly (enlargement of liver and spleen, respectively).

These major symptoms disappear during the convalescent or recovery phase of viral hepatitis. Even in those individuals who recover normally without any long-term, chronic sequelae, feelings of malaise and fatigue may persist for weeks to months. Variations from this generalized picture are described in the discussion of the specific types of viral hepatitis.

Hepatitis A

Hepatitis A virus (HAV) is a small single-stranded RNA virus, which shares some properties with the picornavirus class. It has been shown to exhibit features similar to the enteroviruses. HAV is more resilient to temperature and pH changes than the enteroviruses, however, and is also able to survive in feces and in exudates, and for weeks on inanimate surfaces.

Hepatitis A was formerly known as “infectious hepatitis.” This term is no longer considered an acceptable description of the disease. One of the reasons for the change in terminology has to do with the possible false sense of security people may get by thinking that other viral hepatitis syndromes are not infectious.

Transmission of HAV occurs primarily by the fecal-oral route under conditions of overcrowding, poor personal hygiene, and close contact between infected and non-infected persons. HAV infection is most often indirectly transmitted via contaminated water or food, particularly raw or inadequately cooked shellfish. Common-source outbreaks have occurred in child day-care centers and from food handled by infected food industry

personnel. Blood-borne transmission of HAV can also occur but is very rare. HAV is maintained in the population through serial propagation. A carrier state has not been demonstrated, nor has HAV been shown to result in chronic hepatitis.

The clinical course of hepatitis A ranges from asymptomatic to severe. Fever is often present during acute hepatitis A, but symptoms may last only two to seven days. Sudden onset of the illness is characteristic of HAV. It is highly contagious during its incubation period (two to six weeks) and the early stage of acute disease. Once symptoms develop, viral concentration and the likelihood of transmission decrease.

Two single-antigen Hepatitis A vaccines are currently licensed in the United States for people aged 2 years and older. A formalin-inactivated vaccine, Havrix® (manufactured by GlaxoSmithKline) became available in 1995. After the initial dose, the second dose is given six to twelve months later. The second vaccine is VAQ-TA® and manufactured by Merck & Co. After the initial dose, the second dose is given six to eighteen months later. These vaccines have been shown to be highly effective in producing protective antibodies in studies with both adults and children. It is estimated that the vaccine will protect for at least 20 years.

Twinrix®, a combination vaccine was developed in 2001 to protect against both hepatitis A and hepatitis B. Twinrix® [hepatitis A inactivated & hepatitis B (recombinant) vaccine] is indicated for vaccination of persons aged 18 years and older if there is an indication for both hepatitis A and B vaccination. (Table 1-see page 4)

Persons at increased risk for infection with hepatitis A include:

- travelers to intermediate and high HAV-endemic countries
- men who have sex with men
- illicit drug users
- persons with chronic liver disease, and those who have received or are waiting for liver transplant
- persons who work with HAV-infected primates or work with HAV in the laboratory
- persons who have clotting factor disorders (hemophilia)

Although Hepatitis A vaccination is not routinely recommended for all children in the United States, it is recommended for individuals in the risk groups identified above and for children living in counties and states identified as higher prevalence.

Table 1

Recommended doses of currently licensed formulations of Hepatitis B vaccine, by age group and vaccine type											
Age Group		Single-antigen vaccine				Combination vaccine					
		Recombivax HB		Engerix-B		Comvax*		Pediarix [†]		Twinrix [§]	
		Dose (µg) [¶]	Vol (mL)	Dose (µg) [¶]	Vol (mL)	Dose (µg) [¶]	Vol (mL)	Dose (µg) [¶]	Vol (mL)	Dose (µg) [¶]	Vol (mL)
Infants (<1 yr)		5	0.5	10	0.5	5	0.5	10	0.5	NA ^{**}	NA
Children (1–10 yrs)		5	0.5	10	0.5	5 [*]	0.5	10 [†]	0.5	NA	NA
Adolescents	11–15 yrs	10 ^{††}	1.0	NA	NA	NA	NA	NA	NA	NA	NA
	11–19 yrs	5	0.5	10	0.5	NA	NA	NA	NA	NA	NA
Adults (≥20 yrs)		10	1.0	20	1.0	NA	NA	NA	NA	20 [§]	1.0
Hemodialysis patients and other immuno-compromised persons	<20 yrs ^{§§}	5	0.5	10	0.5	NA	NA	NA	NA	NA	NA
	≥20 yrs	40 ^{¶¶}	1.0	40 ^{***}	2.0	NA	NA	NA	NA	NA	NA

* Combined Hepatitis B–*Haemophilus influenzae* type b conjugate vaccine. This vaccine cannot be administered at birth, before age 6 weeks, or after age 71 months.

† Combined Hepatitis B, diphtheria, tetanus, acellular pertussis adsorbed, inactivated poliovirus vaccine. This vaccine cannot be administered at birth, before age 6 weeks, or at age >7 years.

§ Combined Hepatitis A and Hepatitis B vaccine. This vaccine is recommended for persons aged ≥18 years who are at increased risk for both Hepatitis B virus and Hepatitis A virus infections.

¶ Recombinant Hepatitis B surface antigen protein dose.

** Not applicable.

†† Adult formulation administered on a 2-dose schedule.

§§ Higher doses might be more immunogenic, but no specific recommendations have been made.

¶¶ Dialysis formulation administered on a 3-dose schedule at 0, 1, and 6 months.

*** Two 1.0-mL doses administered at one site, on a 4-dose schedule at 0, 1, 2, and 6 months.

Source: <http://www.cdc.gov/hepatitis/HBV/HBVFAQ.htm>

Diagnosis of hepatitis A infection is confirmed by the identification of HAV antibodies (anti-HAV) in the serum. Early in the course of the disease, the anti-HAV is of the IgM class of immunoglobulins. These antibodies persist for four to six weeks and are then replaced by antibodies of the IgG class. The latter remain in the serum indefinitely and confer permanent immunity to hepatitis A.

Hepatitis B Properties of Virus and Morphological Components

Hepatitis (HBV) is a 42 nanometer (nm) DNA virus containing a complex antigenic structure. This virus has been classified as a member of the Hepadnaviruses, and

is very specific in its colonization requirements, infecting only humans and some primates. This characteristic has limited the development of routine in vitro cultivation techniques for HBV. The viral structure has had to be delineated by detection and identification of specific serologic markers rather than culture of the virus.

The complete virion of Hepatitis B is called the Dane particle. This particle is capable of replication and constitutes the infectious agent. The outer protein coat of the virus, termed hepatitis B surface antigen (HBsAg), is detectable in infected blood and saliva as a surface component of the intact HBV and as freely circulating, noninfectious spherical and tubular forms. These latter particles represent excess HBsAg shed during viral replication. They comprise the major proportion of surface

antigen following infection. This important component was the first serologic marker discovered for HBV. It was initially termed the “Australia antigen” or “Hepatitis-associated antigen (HAA)” by Blumberg and associates. HBsAg remains the major diagnostic antigen for hepatitis B infection.

Resistance

Scientists have accumulated little information regarding the precise inactivation curves of HBV. However, new methods of testing germicides for efficacy in inactivating HBV using the duck hepatitis virus test (DHVT) have been formally recognized by the Environmental Protection Agency (EPA). The duck hepatitis virus is considered an appropriate surrogate organism for testing efficacy in inactivation of the human hepatitis B virus. In recent years, germicide manufacturers have begun to include claims for inactivation of the Hepatitis B virus on label claims. Disinfectants with the ability to destroy *M. tuberculosis* within a ten-minute exposure (i.e., hospital-level, intermediate disinfectants) also are considered capable of inactivating HBV on surfaces.

Transmission

In the 1980’s approximately 260,000 people were infected with the hepatitis B virus in the United States. Since the introduction of the hepatitis B vaccine and improved infection control precautions that number has declined dramatically to an estimated 38,000 total new infections in 2008. There are an estimated 800,000 to 1.4 million people with chronic hepatitis B virus infection in the U.S. Globally, approximately 350,000 people are affected and an estimated 620,000 die each year from hepatitis B.

The disease can be transmitted via direct or indirect modes of cross-infection. HBV has been detected in blood, saliva, semen, and other body secretions and fluids. The direct transmission of this virus to susceptible individuals by contaminated blood or sexual intercourse has been well documented. Vertical transmission from expectant mothers to their offspring at birth is a common mode of HBV infection. When a pregnant woman is also an HBV carrier, passage of the virus to the fetus is very common, with a high risk of induction of an HBV carrier state in the fetus, chronic hepatitis, and eventually, an increased risk for liver cancer. HBV carried in serum may be spread indirectly through blood transfusions or the administration of blood-derived products.

Of particular concern to dental care providers is the information that indicates that improperly sterilized in-

struments, needles, and syringes, when contaminated by blood or blood products, can serve as a source of HBV transmission. As little as 2.5×10^{-5} ml of HBV-contaminated blood (versus 1.0×10^{-2} ml with HAV) has been shown to cause disease. Therefore the use of appropriate methods of sterilization or disposable items should be routine in the practice.

Course of Disease and Diagnosis

Many cases of hepatitis B are not recognized, owing to their asymptomatic or mild course. Approximately 50 to 60 percent of infected individuals develop a sub-clinical infection. When clinically apparent, the disease often has an insidious onset with nonspecific prodromal symptoms such as malaise, fatigue, and anorexia. These symptoms may last for several weeks or up to several months, depending on the extent of HBV infection and the immune status of the host. Anicteric infection (absence of jaundice) is more commonly seen than jaundice and is associated with milder symptoms. Serum transaminase levels indicative of hepatocellular injury may be more than ten times the upper limit of normal values, but are less elevated in milder infections. Symptoms in patients with icteric HBV infection gradually diminish after establishment of jaundice. Full recovery occurs by the end of six months in 90 to 95 percent of patients following acute icteric infection, and by the end of the third or fourth month in 80 percent of the total number of cases.

The development of specific assays for HBV markers has enabled dental health professionals to monitor the course of infection in a quantitative, sensitive manner. Table 2 (see page 9) explains the interpretation of various blood tests available for determining immunity and infectiousness related to the hepatitis B virus.

It is important to note here that the definitive diagnosis of hepatitis B is made by serologically demonstrating the presence of HBsAg. This surface antigen usually is detectable in the blood four to eight weeks after parenteral exposure, but it may appear as early as six days or as late as 24 weeks. HBsAg becomes detectable before clinical symptoms of hepatitis and before any other abnormal lab findings. Serologic levels of HBsAg may peak and actually begin to decline by the time the patient first becomes visibly ill. It is therefore very important to test for the presence of HBsAg as soon as the diagnosis of hepatitis B is suspected. After a variable interval of weeks to months, most patients begin to recover, with HBsAg rapidly becoming undetectable as transaminase enzymes and bilirubin concentrations return to normal. Specific antibody against the core antigen (anti-HBc) appears

while HBsAg is still evident. In contrast, synthesized immunoglobulins to HBsAg (anti-HBs) correlate well with the development of protective immunity against HBV.

The significance of anti-HBs in an unvaccinated individual's serum may be summarized as follows:

- denotes a previous clinical or subclinical infection with HBV;
- in most cases means the person has recovered from hepatitis B infection, and is probably immune to reinfection.

Hepatitis B Carrier State and Chronic Hepatitis B

Infection with HBV results in a prolonged carrier state in 5 to 10 percent of infected persons. Surprisingly, the carrier condition is more frequently seen following milder anicteric disease. The majority of HBV carriers are asymptomatic and are frequently unaware of having had the disease, but they can transmit HBV via blood, bloody saliva, whole saliva, semen, and other secretions. These individuals continue to produce virus although they appear asymptomatic. The presence of HBsAg is most often used to identify the individual likely to transmit HBV infection. The persistence of hepatitis B antigen (HBeAg) levels is also used as a criterion of high patient infectivity, and an increased potential to transmit disease. In addition, the possibility exists for potential HBV transmission by individuals having HBsAg at undetectable levels but high titers of anti-HBc in the absence of anti-HBs.

Approximately 20 to 30 percent of HBV carriers have evidence of chronic hepatitis with laboratory or histologic evidence of continued hepatocellular damage. Chronic hepatitis B exists as two morphologic variants: chronic persistent hepatitis and chronic active hepatitis. The former is characterized by inflammatory infiltration and expansion of the portal tracts, minimal fibrosis, and normally appearing parenchymal cells. Chronic active hepatitis is characterized by irregular necrosis of the hepatic parenchymal cells and may gradually progress to cirrhosis. In recent years, treatments with injected interferon and other antivirals have shown some success in eradicating the HBV carrier state. While not universally used, interferon can demonstrate a 40 to 50 percent effectiveness in eradicating this chronic, possibly lifelong condition.

Hepatitis C Virus Introduction

Hepatitis C virus (HCV) is the most common chronic bloodborne infection in the United States. Throughout

the 1980's there were an average of 242,000 new infections each year. Since the introduction of reliable blood tests in the early 1990's and subsequent tissue, donor organ and donor blood screening, by 1996 that number had dropped to about 36,000 new cases each year. Most of the estimated 3.9 million Americans infected with HCV are chronic carriers who are at an increased risk for chronic liver disease. Many chronically infected individuals are unaware of their infection and do not have symptoms of clinical illness. (Figure 1)

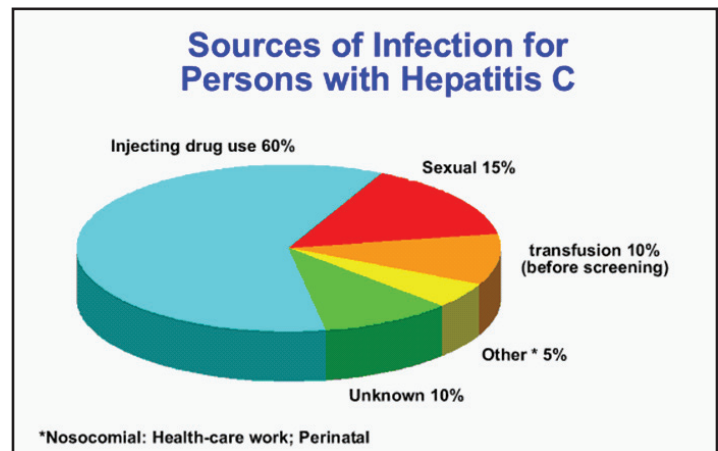


Figure 1 -Centers for Disease Control and Prevention

Transmission and Symptoms

Risk factors that have been associated with transmission of HCV and the following people will be at a higher risk to acquire HCV:

- recipients of clotting factor concentrates made before 1987
- recipients of blood transfusions or organ transplants before July 1992
- current or former injection drug users
- chronic hemodialysis patients
- those already infected with HIV, and children born to HCV + mothers
- health care workers involved in exposures
- recipients of blood or organs from a donor that has since tested HCV +

Medical and dental procedures, foreign travel, piercing and tattooing have not been implicated in increased risk for transmission.

About 80% of infected individuals will have no clinical symptoms of HCV. Symptoms that may occur include jaundice, fatigue, dark urine, abdominal pain, loss of appetite, fever, clay-colored stool, joint pain, nausea, and vomiting.

Prevention

For the general population, prevention efforts are targeted at avoidance of high-risk activities such as unprotected sex with multiple partners and the use of shared needles for injecting drugs.

Healthcare workers who have exposure to blood are at risk for infection with any of the bloodborne pathogens. Prevalence of HCV infection among healthcare workers has not been found to be greater than the prevalence among the general population. The average incidence of anti-HCV seroconversion after accidental percutaneous exposure from an HCV-positive source is 1.8% (range: 0%--7%). In contrast to HBV, the epidemiological data for HCV suggest that environmental contamination with blood containing HCV is not a significant risk for transmission in the health-care setting. For these reasons, adherences to standard precautions are considered adequate in controlling the spread of HCV from worker to patient, patient to worker and patient to patient. No work restrictions are recommended for HCV-infected healthcare workers.

Postexposure Management

Postexposure protocols for exposures to blood should include considerations for HCV exposure. Source patient testing to determine if exposure to HCV has occurred is an important element of the exposure follow-up. Early identification of infection presents an opportunity for early identification of chronic disease and referral for appropriate treatment. Postexposure follow-up should be conducted by a qualified medical professional that is aware of current recommendations for testing and postexposure prophylaxis medication. As of this writing, no antiviral agents have been approved or recommended for use following an exposure to HCV-infected blood. Additionally, no vaccine is currently available for prevention of transmission.

Hepatitis D (Delta Hepatitis)

Hepatitis D originally was called delta hepatitis following its discovery by Rizzetto and colleagues in 1977. As subsequent investigations isolated and characterized the etiologic agent, it became apparent that hepatitis D virus (HDV) was distinctly different from HBV and the other hepatitis viruses. HDV is a defective RNA virus, which is unique in its inability to accomplish its own replication within infected hepatocytes. This microorganism requires HBV to function as a helper virus by providing a surface coat protein (HBsAg) necessary for synthesis of progeny viruses. In a real sense HDV may

be considered a “parasite of HBV,” and its epidemiology closely parallels that of HBV.

Outbreaks of HDV have been reported in the U.S., the largest of which occurred in Worcester, Massachusetts. More than 700 cases of hepatitis were diagnosed between 1983-1988 in that area, with more than 65 patients testing positive for HDV. Of the 14 deaths attributed to this outbreak, 11 were HDV-positive. In February of 2009, The National Institutes of Health (NIH) reported that 15 million people worldwide are infected with HDV.

HDV is spread primarily through shared needles. Patients that are known to be HBV positive should be counseled on the prevention of HDV contraction and the increased exposure to HDV when abusing IV drugs and sharing needles.

Infection with HDV occurs via two modalities: 1) simultaneous co-infection with HBV, and 2) superinfection in hepatitis B carriers. The most common outcome of simultaneous HBV and HDV infection is an episode of acute hepatitis followed by recovery from both viral infections. Fulminant hepatitis develops in occasional cases. In HDV superinfection in HBsAg carriers, the dually infected individuals are more likely to have serious, possibly fatal, acute fulminant hepatitis.

Hepatitis E Virus

Hepatitis E virus (HEV) is a major etiologic agent of enterically transmitted non-A, non-B hepatitis worldwide. Clinically, it is most closely associated with Hepatitis A in that it is passed through contaminated water and food supplies. As such, it should not be considered an increased risk for occupational transmission in the dental setting. The incubation period following exposure can range from 15-60 days. Virus excretion in the stools appears to continue for about 2 weeks after its first appearance. The symptoms are similar to those for other hepatitis viruses in that the patient may experience abdominal pain, anorexia, dark urine, fever, hepatomegaly, jaundice, malaise, nausea, and vomiting. The mortality rate is very low with HEV. No chronic phase is associated with hepatitis E virus, meaning that once a patient recovers, they do not continue to be at risk for subsequent liver disease due to the infection, nor do they continue to pose a transmission threat.

Contaminated drinking water is the most commonly documented vehicle of transmission for HEV, rather than person to person contact. Hepatitis resulting from exposure to HEV in the United States has been limited to individuals with recent travel to HEV-endemic areas of the world rather than exposure domestically.

Non A-E Hepatitis

In 2000, new isolates of hepatitis were found, designated hepatitis F (HFV), hepatitis G virus (HGV) and transfusion transmitted virus (TTV). As of 2010, the etiology of the disease is still unknown and to date this agent has not been associated with any cases of acute or chronic hepatitis. The CDC has determined it will not routinely test for this virus unless it is shown to be associated with acute or chronic disease. Additionally, no suitable diagnostic tests exist to detect the presence of these viruses. As patients continue to present with strains of hepatitis that cannot be specifically classified, they are categorized in either the non A-E hepatitis or Hepatitis F, G, or H categories.

IMMUNOLOGICAL PREVENTION OF DISEASE

Artificial Passive Immunity

Hepatitis B immune globulin (HBIG) has been used in certain defined circumstances. These include: needle-stick or mucous membrane exposures in susceptible individuals with blood from an HBsAg positive individual, and in conjunction with hepatitis B vaccine for a newborn whose mother either has contracted active hepatitis B during pregnancy or is a chronic HBV carrier. HBIG is prepared from the plasma of individuals known to have circulating anti-HBsAg. This commercial product contains approximately 1 to 2x10⁴ times more of this specific antibody than ISG, and therefore is preferred in the immunoprophylaxis of hepatitis B.

Artificial Active Immunity—Hepatitis B Vaccines

Plasma-derived vaccines

The search for a successful vaccine against hepatitis B began in the late 1960s. Krugman and co-workers demonstrated that infective serum (strain MS-2), containing HBV diluted 1:10 in distilled water and heated to 98°C for one minute, prevented or modified the disease in approximately 70 percent of susceptible individuals. The MS-2 serum contained large quantities of hepatitis B surface antigen (HBsAg). Much of the subsequent work focused on the extraction and purification of this non-infectious, viral coat protein for use as the vaccine preparation. This effort was fostered by the observation that replication of hepatitis B virus in infected individuals was not nearly as efficient as the large amounts of excess coat proteins synthesized and passed into the circulation. As patients recovered from viral infection,

antibodies to this antigen (anti-HBs) appeared and were protective against recurrent viral attack.

Accumulated evidence also indicated that these HBsAg forms are present in high concentration in carriers of hepatitis B. Thus, carriers with high serum HBsAg titers were originally shown to provide a supply of viral antigen for the production of the first commercially available form of the vaccine. This achievement was crucial to the overall effort, because hepatitis B virus has not yet been routinely cultured *in vitro*.

Ultracentrifugation was found to be a very effective means for large-scale isolation of HBsAg from asymptomatic hepatitis B carriers. Additional chemical treatment of the isolated surface proteins with the enzyme pepsin, concentrated urea, and formalin was designed to inactivate any residual HBV particles or particles of any other possible virus, and to remove any residual traces of plasma protein as well. These measures produced a vaccine suitable for administration to human beings.

With refinement of the original vaccine (addition of alum as an adjuvant to increase vaccine immunogenicity), it became apparent that an effective prophylactic weapon had been developed. One of the clinical trials with this vaccine assessed its efficacy in a placebo-controlled, randomized, double blind study in 1983 with homosexual men known to be at high-risk for hepatitis B. The vaccine was found to induce high titers of anti-HBs in injected persons (77 percent after primary dose, 96 percent after booster). Of prime importance was the observation that during an 18-month follow-up interval, 18 to 27 percent of the placebo recipients developed clinical or subclinical hepatitis B while only 1.4 to 3.4 percent of the HBsAg-vaccinated subjects did so.

Heptavax-B, the vaccine (Merck and Company), was released for commercial use in 1982. This preparation is a sterile suspension for intramuscular injection. Each 1.0 ml dose of vaccine contains 20 µg of hepatitis B surface antigen formulated in an alum adjuvant, and thimerosal (a mercury derivative) 1:20,000 as a preservative. It was used for immunization against all known subtypes of hepatitis B virus, but did not prevent infection caused by hepatitis A, hepatitis C, or hepatitis E viruses. Subsequent infection with HDV was prevented, however, as hepatitis D cannot develop in individuals who are protected from hepatitis B infection.

The preparation is given in a regimen of three 1.0 ml intramuscular doses. The second and third doses followed one and six months, respectively, after the first. No serious side effects have been attributed directly to parenteral injection of the vaccine. Mild, short-term ef-

fects include soreness at the injection site, fever, flu-like symptoms and general malaise. With the development, approval, and marketing of second generation hepatitis B vaccines which do not use plasma from HBV carriers, the original Heptavax–B is currently available only in limited amounts and is reserved for patients with specific medical conditions.

Recombinant (Single-Antigen) DNA Vaccines

The first clinical vaccine prepared using recombinant (produced from a cloned gene) DNA technology was licensed in 1986, and made available for general use in 1987. Recombivax HB (Merck and Company) was developed initially as a newer vaccine to provide an alternative to the plasma-derived vaccine.

This preparation is produced in cultures of *Saccharomyces cerevisiae* (common baker’s yeast), into which a plasmid containing the gene for HBsAg has been inserted. HBsAg is subsequently harvested after lysis of cultured yeast cells. Administered vaccine is designed to contain 10 micrograms (µg) of HBsAg protein per milliliter, absorbed with 0.5 milligrams per ml of aluminum hydroxide (alum), with thimerosal as a preservative.

The immunogenicity of Recombivax HB is comparable to that observed for the plasma-derived preparation. In 1989 Smith, Kline, Beecham received a license in the U.S. for their Engerix-B vaccine. The major difference between the products is the number of steps used

in recovery and purification of the antigen from the yeast cultures, which results in different dosage amounts. Both vaccine preparations provide adequate immunity. Table 1 includes a chart of the recommended dosage and timeline for receiving the Hepatitis B vaccines.

Combination Vaccines

Combination vaccines have been developed that combine an HBV vaccine with other vaccines. The Comvax, Pediarix, and Twinrix combination vaccines have been combined with other vaccines to reduce the number of injections for infants and children. See Table 1 (page 4) for recommended dosages and timelines.

Testing for Immunity

After receiving a series of Hepatitis B vaccinations, the healthcare professional should receive a blood test (anti-body titer) to verify their immunity. Most will sero-convert after receiving the standard recommended protocol. However, there are cases when a person will not receive immunity and will need an additional injection, or even a repetition of the full series.

For an adult, the titer should be drawn 1 – 2 months after the series was completed. When the results are returned, the results should come back the worker is positively immune to Hepatitis B. Unfortunately, laboratory results can be worded differently and can be misinterpreted. Table 2 can be used to interpret received results.

Table 2

Interpretation of the Hepatitis B Panel		
Tests	Results	Interpretation
HBsAg anti-HBc anti-HBs	negative negative negative	susceptible
HBsAg anti-HBc anti-HBs	negative positive positive	immune due to natural infection
HBsAg anti-HBc anti-HBs	negative negative positive	immune due to hepatitis B vaccination
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive positive negative	acutely infected
HBsAg anti-HBc IgM anti-HBc anti-HBs	positive positive negative negative	chronically infected
HBsAg anti-HBc anti-HBs	negative positive negative	four interpretations possible *

* 1. May be recovering from acute HBV infection.
 2. May be distantly immune and test not sensitive enough to detect very low level of anti-HBs in serum.
 3. May be susceptible with a false positive anti-HBc.
 4. May be undetectable level of HBsAg present in the serum and the person is actually a carrier.

Source: Centers for Disease Control and Prevention

RECOMMENDATIONS FOR INFECTION CONTROL PROCEDURES

This course was not designed primarily to include a comprehensive section on infection control precautions. However, it is appropriate to include a summary description of current infection control recommendations.

Effective infection control must occur as a routine component of professional activity. The use of standard precautions to manage all patients minimizes occupational exposure to microbial pathogens by addressing the reality that most potentially infectious individuals are asymptomatic and therefore undiagnosed. This has already been discussed in terms of various types of viral hepatitis. The medical history should not be used to definitively identify the "infectious disease risk" of a patient. Every patient must therefore be considered infectious and the same infection control procedures applied for all patients. Unfortunately, this concept of standard precautions is a difficult one for some dental professionals to put into practice. However, when standard precautions are used, additional procedures are not necessary when treating a patient who is known to have an infectious disease.

The importance of these precautions in applying professional organization recommendations, Centers for Disease Control and Prevention guidelines, and the OSHA standard must be considered. Develop an organized, comprehensive program with input from all dental professionals in the clinical setting. Determine the infection control strengths of your practice and build on them by integrating new knowledge into the practice routine.

The change from the initial 1978 ADA recommendations to the present has been great, and other modifications probably will be made for the next few years. It is therefore essential for dental professionals to remain current in this topic, as developments in infection control continue to provide better products and advances in asepsis technology.

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The Test

Now proceed to the test. All questions are constructed using a multiple-choice format.

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HEPATITIS: WHAT EVERY DENTAL PROFESSIONAL SHOULD KNOW POSTTEST

Choose the one best answer.

1. 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
2. Persons with increased risk for infection with Hepatitis A include _____.
 - A. persons who have clotting factor disorder.
 - B. illicit drug users
 - C. travelers to intermediate and high HAV-endemic countries
 - D. persons with chronic liver disease
 - E. all of the above
3. Germicides are tested for efficacy against Hepatitis B virus using _____.
 - A. purified human Hepatitis B virus.
 - B. duck Hepatitis virus
 - C. bovine Hepatitis virus
 - D. none, germicides are not tested for efficacy against Hepatitis B virus
4. _____ of individuals infected with HBV become chronic carriers.
 - A. 1%-5%
 - B. 5%-10%
 - C. 10%-15%
 - D. 15%-20%
5. _____ immunity is conferred by the administration of Hep B vaccine.
 - A. Artificial active
 - B. Artificial passive
 - C. Natural passive
 - D. Natural active
6. Hepatitis A can be characterized as _____.
 - A. transmitted primarily via the fecal-oral route
 - B. transmitted primarily through contaminated blood transfusions
 - C. transmitted primarily through unprotected sex
 - D. transmitted primarily through illicit injection drug use
7. _____ may be traced to contaminated food or water, especially inadequately cooked shellfish.
 - A. Hepatitis A
 - B. Hepatitis B
 - C. PT-NANB
 - D. both A and B
 - E. all of the above
8. _____ is least likely to include jaundice as a clinical symptom.
 - A. Hepatitis A
 - B. Hepatitis B
 - C. Hepatitis C
 - D. Hepatitis D
9. The term "infectious" hepatitis is no longer used, but was formerly considered a synonym for _____.
 - A. hepatitis A
 - B. hepatitis B
 - C. hepatitis C
 - D. A, B and C
10. The outer protein coat of the virus, termed hepatitis B surface antigen (HBsAg), is detectable in infected blood and saliva as a surface component of the intact HBV. Disinfectants with the ability to destroy *M. tuberculosis* within a ten-minute exposure are NOT capable of inactivating HBV on surfaces.
 - A. Both statements are true
 - B. First statement is true. Second statement is false.
 - C. First statement is false. Second statement is true.
 - D. Both statements are false.

11. HBV can be transmitted through direct contact. HBV can be transmitted through indirect contact.
- Both statements are true.
 - First statement is true. Second statement is false.
 - First statement is false. Second statement is true.
 - Both statements are false.
12. After receiving the Hepatitis _____ vaccination, healthcare professionals should receive an antibody titer to verify their _____.
- A/ infectivity
 - C/ immunity
 - B/ infectivity
 - B/ immunity
13. A symptom of jaundice in a patient may suggest _____.
- drug-induced hepatitis
 - type A hepatitis
 - type B hepatitis
 - ET-NANB hepatitis
 - any of the above
14. As patients recovered from hepatitis B, antibodies to the antigen (anti-HBs) were found causing protection to future attacks. HBsAg forms are present in low concentration in carriers of hepatitis B.
- Both statements are true.
 - First statement is true. Second statement is false.
 - First statement is false. Second statement is true.
 - Both statements are false.
15. Risk factors associated with Hepatitis C include _____.
- dental and medical procedures
 - piercings and tattoos
 - blood transfusions and injected drug use
 - all of the above
16. The most important serologic marker employed in the diagnosis of hepatitis B infection and its chronic sequelae, is _____.
- HBsAg
 - HBcAg
 - HBeAg
 - transaminase
17. Medical histories are the best way to determine if a patient is an infectious disease risk. The same infection control procedures should be applied for every patient.
- Both statements are true.
 - First statement is true. Second statement is false.
 - First statement is false. Second statement is true.
 - Both statements are false.
18. A physician reports to you that a patient had a positive "Australia antigen" determination in 1976. This test has to do with the diagnosis of _____.
- hepatitis D
 - hepatitis A
 - both choice A and B
 - neither choice A nor B
19. The Dane particle is _____.
- hepatitis A virus
 - hepatitis B virion
 - hepatitis C particle
 - inclusion of hepatitis A virus
 - DNA polymerase enzyme
20. Hepatitis D appears _____.
- As a co-infection or superinfection associated with Hepatitis B
 - As a co-infection or superinfection associated with Hepatitis C
 - As a co-infection or superinfection associated with Hepatitis A
 - As an infection independent of any other Hepatitis virus
21. The hepatitis B serologic marker _____ is most associated with infectivity of hepatitis B infection.
- HBsAg
 - HBcAg
 - HBeAg
 - bilirubin levels in urine
 - transaminase
22. Hepatitis conditions are generally divided into _____ stages.
- prodromal, icteric, and convalescent
 - acute, chronic, and necrosis
 - inflammation, jaundice, and malaise
 - enteral, parenteral, and fulminant

23. Clinical signs of jaundice can be detected on the _____.

- A. nail beds
- B. skin, sclera
- C. gingiva
- D. all of the above

24. With HBV, a full recovery occurs by the end of _____ in 90–95% of patients.

- A. 9 weeks
- B. 6 months
- C. 9 months
- D. 12 months

25. Hepatitis _____ is the most common chronic bloodborne infection in the United States.

- A. A
- B. B
- C. C
- D. D