Chapter 14
Hepatitis B

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Hepatitis B Infection

Etiology

Hepatitis B virus (HBV), a member of the *Hepadnaviridae* family, in the genus *Orthohepadnavirus* is the cause of hepatitis B infection, a disease primarily affecting the liver. Virions consist of partially double-stranded DNA inside an icosahedral nucleocapsid that is surrounded by an outer lipid envelope. Small, medium, and large surface proteins embedded in the outer lipid envelope are necessary for the virus to attach to and enter a target cell to initiate infection. Envelope protein lines the inner aspect of the lipid envelope, and core protein forms the viral capsid. The three proteins are more commonly referred to as hepatitis B surface antigen (HBsAg), hepatitis B core antigen (HBcAg), and hepatitis B e antigen (HBeAg) because under the right circumstances, they are capable of stimulating an immune response in the infected individual. Individuals who mount an effective immune response to the virus during the acute hepatitis B disease clear the infection. Those who go on to develop chronic hepatitis B infection have a lifelong risk of developing hepatocellular carcinoma, cirrhosis, and liver failure.

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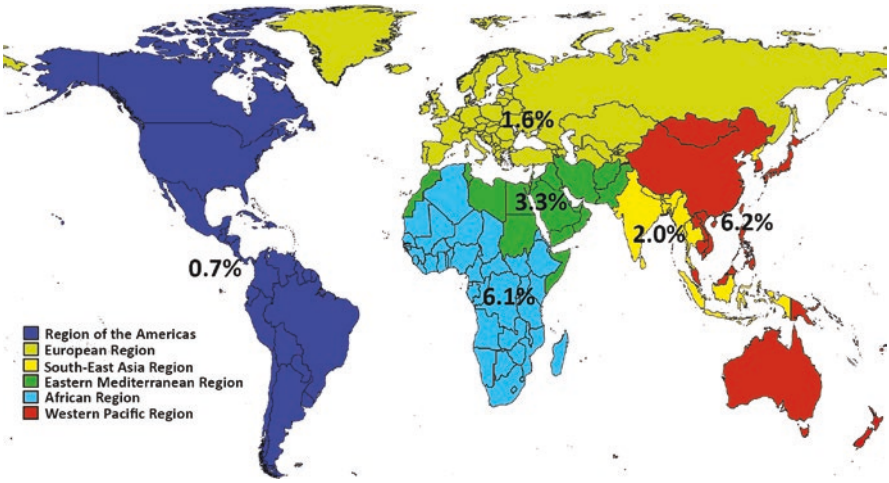

Fig. 14.1 Prevalence of hepatitis B infection in each of the six World Health Organization regions

Global Epidemiology of Hepatitis B

Hepatitis B disease is a major public health problem everywhere in the world. The burden of infection varies by country and by geographic location with the heaviest affected areas experiencing disease in 15% or more of their total population. The global distribution of disease burden can be appreciated by viewing the mean prevalence of hepatitis B infection across each of the six World Health Organization regions (Fig. 14.1). High-intermediate to high endemicity of hepatitis B, defined as a prevalence of 5% to greater than 8%, is seen across the Western Pacific (6.2%) and Africa regions (6.1%), with some countries reporting disease prevalence higher than 15%. Low to intermediate endemicity, defined as a prevalence of 2% to <5%, is seen in the Eastern Mediterranean (3.3%) and Southeast Asia regions (2.0%), while low endemicity (<2%) is seen in the regions of Europe (1.6%) and the Americas (0.7%) (Fig. 14.1).

Epidemiology of Hepatitis B in the United States

Acute hepatitis B infection rates have remained steady in the United States at 1.0 per 100,000 population since 2009. Rates among those living in nonurban areas are somewhat higher than for urban areas. Acute infection rates are highest among adult African Americans. Between 2006 and 2013, the state health departments of Kentucky, Tennessee, and West Virginia all reported steady increases in acute HBV infection among non-Hispanic Caucasians between 30 and 39 years of age. This somewhat isolated spike in acute disease activity was determined to be caused by exposures to contaminated drug paraphernalia and sharing of needles used to inject illicit substances.

Chronic hepatitis B infection also causes substantial morbidity and mortality in the United States. The 2011–2012 National Health and Nutrition Examination Survey indicated that 850,000 Americans were living with chronic hepatitis B infection at the time. By 2020, estimates of the chronic disease burden exceeded one million individuals. Non-Hispanic Asians account for nearly half of these chronic hepatitis B infections despite representing only 5% of the US population. As many as 70% of those chronically infected are foreign-born immigrants from highly endemic areas of the world. Each year, 2,000 Americans die from complications of chronic hepatitis B infection.

Transmission of Hepatitis B

Hepatitis B is transmitted from person to person via percutaneous or mucous membrane exposure to infected blood or body fluids. Possible modes of horizontal transmission include sexual contact; sharing of razors, toothbrushes, or injection drug paraphernalia; tattooing; body piercing; scarification or acupuncture using contaminated needles; and occupational exposure to blood. Perinatal transmission is very common in highly endemic regions of the world, accounting for the majority of new cases worldwide. Infants born to infected mothers who test positive for both HBsAg and HBeAg during pregnancy are at the highest risk of acquiring infection perinatally. In Asia, the risk of the infant becoming infected is close to 100%. Infants born to mothers who test positive for HBsAg and negative for HBeAg have a 5–30% risk of being infected. Young age at the time of the acute infection is an independent risk factor for developing chronic infection. Most newborns infected perinatally become chronically infected.

The average incubation period for HBV is 75 days, with a range of 30–180 days.

Clinical Presentation of Hepatitis B Infection

More than half of older children and adults infected with hepatitis B and virtually all perinatally infected newborns are asymptomatic. Others present with nonspecific signs and symptoms typical for many acute viral infections including fever, fatigue, loss of appetite, nausea, vomiting, and muscle, joint, and/or abdominal pain. The possibility of hepatitis B infection may not be considered unless or until the patient develops signs that are more specific for acute viral hepatitis, such as jaundice of the eyes or skin, tea- or cola-colored urine, right upper quadrant abdominal pain, hepatomegaly, and clay-colored stools. In those who undergo laboratory testing as part of their diagnostic evaluation early in the illness, results will be consistent with hepatic inflammation, showing elevated serum hepatic transaminases with or without hyperbilirubinemia.

Rarely, acute infection with HBV causes acute, fulminant hepatic necrosis with liver failure. Without liver transplantation, this condition is usually fatal. Overall, the mortality associated with acute HBV infection is about 1%. Laboratory evidence of acute infection includes positive tests for HBsAg and anti-HbcAg IgM. Results of HBeAg testing may also be positive. Individuals who test positive for HBeAg are highly contagious.

The likelihood that an individual will develop chronic HBV infection is age-dependent.

Most infants infected perinatally, and between 80% and 90% of children who are infected horizontally during the first year of life become chronically infected. The risk of chronic infection drops below 50% among those infected between the ages of 1 and 6 years and to less than 5% of those who acquire infection as an adult.

Chronic HBV disease is defined as the persistence of HBsAg in the blood for more than 6 months. Between 20% and 30% of individuals with chronic HBV infection develop cirrhosis, liver failure, or hepatocellular carcinoma. Patients typically remain asymptomatic until one of these complications develops. In 2015, an estimated 887,000 individuals worldwide died from complications of hepatitis B infection.

Management

Specific treatment is not available for acute HBV infection. Management includes symptomatic care, with intravenous fluid replacement, as needed.

Individuals with chronic HBV infection require lifelong medical care. Alcohol consumption and coinfection with hepatitis C and/or D negatively impact HBV morbidity and mortality. Patients should avoid medications, including those available over the counter, that are potentially hepatotoxic. Vaccination against hepatitis A should be administered to susceptible individuals. Several antiviral medications, including tenofovir and entecavir, are now available for the treatment of chronic HBV infection, with the goal of virus suppression. Curative antiviral regimens have not yet been identified. Only 10% of treatment-eligible people receive antiviral therapy.

Prevention: Hepatitis B Vaccine

Hepatitis B infection and its complications are vaccine-preventable conditions. Safe and highly effective vaccines that provide long-lasting protection have been available since 1982. Vaccine-induced immunity provides protection against infection for at least 30 years. WHO has recommended that hepatitis B vaccine be included in all national immunization schedules since 1991. Suboptimal adherence to the recommended three-dose regimen, especially in highly endemic areas and in certain high-risk populations, remains problematic.

Vaccines Available in the United States

All currently available HBV vaccines are recombinant formulations of HBsAg. The vaccine-derived HBsAg is easily detected in blood samples of individuals who have been recently vaccinated. Since serum HBsAg testing is used as a diagnostic marker for HBV infection, it is important to understand that available assays may be able to detect vaccine-derived HBsAg for as long as 28 days postvaccination.

Three monovalent formulations (Recombivax HB, Engerix-B, Heplisav-B) and three combination formulations (Pediarix, Twinrix, Vaxelis) of HBV vaccine are approved and available for use in the United States.

Available Monovalent Hepatitis B Vaccines

Recombivax HB, marketed by Merck's Vaccine Division, was FDA approved in 1986 for all ages as a three-dose series. The standard doses for children and adults are 5 mcg in 0.5 mL and 10 mcg in 1 mL, respectively. Doses are administered intramuscularly, except in patients with hemophilia where the subcutaneous route is preferred. The higher dose of 40 mcg is recommended for adults who are undergoing dialysis because of its superior immunogenicity in this high-risk population. Prefilled syringes containing single doses are available as 5 mcg/0.5 mL, 10 mcg/1 mL, and 40 mcg/1 mL.

Engerix-B, marketed by GlaxoSmithKline, was FDA approved in 1989 for all ages as a three-dose series. The standard doses for children and adults are 10 mcg in 0.5 mL and 20 mcg in 1 mL, respectively. Doses are administered intramuscularly, except in patients with bleeding disorders where the subcutaneous route may be considered. The higher dose of 40 mcg is recommended for adults who are undergoing dialysis. Prefilled syringes containing single standard doses are available as 10 mcg/0.5 mL and 20 mcg/1 mL. Adults on hemodialysis should be immunized with 2 mL of the 20 mcg/1 mL formulation for each dose.

Heplisav-B, marketed by Dynavax, was FDA approved in 2017 for use in adults as a two-dose series. The standard dose is 20 mcg in 0.5 mL. It has not been studied in adults receiving hemodialysis.

Available Combination Hepatitis B Vaccines

Twinrix, marketed by GlaxoSmithKline, was FDA approved in 2001 for use in adults. Twinrix is a bivalent combination vaccine derived from the monovalent products Engerix-B and Havrix used to immunize adults against hepatitis B and hepatitis A (see Chap. 35). The 1 mL unit dose formulation includes 20 mcg of HBsAg and 720 ELISA units of inactivated hepatitis A.

Pediarix, marketed by GlaxoSmithKline, was FDA approved in 2002 for use in children of ages 6 weeks through 6 years. Pediarix is a pentavalent combination vaccine used to immunize infants and young children against diphtheria, tetanus, pertussis, polio, and hepatitis B (see Chap. 35). Each 0.5 mL unit dose formulation contains 25 Lf units of diphtheria toxin, 10 Lf units of tetanus toxoid, 25 mcg of inactivated pertussis toxin, 25 mcg of filamentous hemagglutinin, 8 mcg of pertactin, 40 D-antigen units (DU) of type 1 poliovirus, 8 DU of type 2 poliovirus, 32 DU of type 3 poliovirus, and 10 mcg of HBsAg. A three-dose series may be given to infants born to HBsAg-negative mothers who already received a birth dose monovalent hepatitis B vaccine.

Vaxelis, co-marketed by Sanofi Pasteur and Merck's Vaccine Division, was FDA approved in 2018 for use in children of ages 6 weeks through 4 years. Vaxelis is a hexavalent combination vaccine used to immunize infants and young children against diphtheria, tetanus, pertussis, polio, hepatitis B, and *Haemophilus influenzae* type b (see Chap. 35). Each 0.5 mL unit dose formulation contains 15 Lf units of diphtheria toxin, 5 Lf units of tetanus toxoid, 20 mcg of detoxified pertussis toxin, 20 mcg of filamentous hemagglutinin, 3 mcg of pertactin, 5 mcg of fimbriae types 2 and 3, 29 DU of type 1 poliovirus, 7 DU of type 2 poliovirus, 26 DU of type 3 poliovirus, 10 of mcg HBsAg, and 3 mcg of polyribosylribitol phosphate bound to 50 mcg of the outer membrane protein complex of *Neisseria meningitidis*. A three-dose series may be given to infants born to HBsAg-negative mothers and who received a dose of any HBV vaccine prior to or at 1 month of age.

Immunizing Antigen

All available hepatitis B vaccines use recombinant HBsAg as the immunogen. The HBsAg included in Recombivax HB and Vaxelis is derived from a recombinant strain of the yeast *Saccharomyces cerevisiae* that encodes HBsAg. Yeast are grown on complex culture media containing yeast extract, soy peptone, dextrose, amino acids, and mineral salts. Recombinant HBsAg is released from the yeast cells by disruption and then purified using a series of physical and chemical methods. Purified HBsAg is treated with formaldehyde and then coprecipitated with aluminum hydroxyphosphate sulfate (alum) as the adjuvant.

Similarly, the recombinant HBsAg used in Engerix-B, Twinrix, and Pediarix is derived from genetically modified *Saccharomyces cerevisiae*. Recombinant HBsAg is purified using several physiochemical steps before being adsorbed onto aluminum hydroxide adjuvant.

The recombinant HBsAg used in Heplisav-B is expressed by a recombinant strain of *Hansenula polymorpha* yeast. The yeast are grown in a chemically defined fermentation medium containing vitamins and mineral salts. Recombinant HBsAg is released by cell disruption and purified physiochemically. Purified HBsAg is then combined with CpG 1018 adjuvant, a 22-mer phosphorothioate-linked oligodeoxynucleotide in phosphate-buffered saline.

Additives and Excipients

Recombivax HB contains less than 1% yeast protein, approximately 0.5 mg/mL of aluminum, and less than 15 mcg/mL of residual formaldehyde. The tip caps of the prefilled syringes contain natural rubber latex. Recombivax HB is preservative-free.

Engerix-B contains less than 5% yeast protein, 0.25 mg aluminum hydroxide, 9 mg/mL sodium chloride, 0.98 mg/mL disodium phosphate dihydrate, and 0.71 mg/mL sodium dihydrogen phosphate dihydrate. The tip caps of the prefilled syringes contain natural rubber latex. Engerix-B is preservative-free.

Heplisav-B contains less than 5% yeast protein, less than 20 pcg yeast DNA, less than 0.9 ppm deoxycholate, 3000 mcg CpG1018 per 20 mcg HBsAg, 9 mg/mL sodium chloride, 1.75 mg/mL sodium phosphate dibasic dodecahydrate, 0.48 mg/mL sodium phosphate monobasic dihydrate, and 0.1 mg/mL polysorbate 80. Heplisav-B is latex-free and preservative-free.

For a summary of additives and excipients included in Twinrix, Pediarix, Vaxelis, see Chaps. 4 and 35.

Vaccine Recommendations

Hepatitis B Vaccine Recommendations: Pediatrics

Guidance for the use of hepatitis B vaccine has been updated and expanded since the US Advisory Committee on Immunization Practices (ACIP) first published recommendations in 1991. Currently, a dose of monovalent hepatitis B vaccine is recommended for all infants within 24 hours of birth followed by two or three doses of monovalent or hepatitis B-containing combination vaccine to complete the series, usually by 6 months of age. The birth dose helps to ensure protection against perinatal transmission.

All newborns should receive their first dose of hepatitis B vaccine shortly after birth. Two important factors influencing the details of this recommendation are the mother's hepatitis B status and the weight of the infant. Medically stable newborns born to mothers who are known to be HBsAg negative and who weigh 2000 grams (4 lbs. 7 oz) or more should receive a dose of monovalent hepatitis B vaccine within 24 hrs of birth.

Infants born to HBsAg-negative mothers who weigh less than 2000 grams should receive their birth dose of vaccine when they reach a chronological age of 1 month or at the time of hospital discharge, whichever comes first. All infants born to HBsAg-positive mothers, regardless of weight, should receive one dose of hepatitis B vaccine and 0.5 mL of hepatitis B immune globulin (HBIG) at different injection sites within 12 hours of birth.

Those infants weighing less than 2000 grams when they receive their first dose of the vaccine require three additional doses of vaccine (four doses total) starting when they reach a chronological age of 1 month. All infants born to mothers with unknown HBsAg status, regardless of weight, should receive one dose of vaccine within 12 hours of birth. If they weigh less than 2000 grams, they should also receive 0.5 mL of HBIG within 12 hours of birth plus three additional doses of vaccine (four total) beginning at 1 month of age. For those weighing 2000 grams or more, HBIG administration can be delayed for up to 7 days of age while awaiting test results of maternal HBsAg status.

Under most circumstances, the hepatitis B vaccine series is completed by administering a total of three doses. Dose 1 is given at birth, dose 2 is given at 1–2 months, and dose 3 is given at 6–18 months of age. If no birth dose was given, the three-dose series should be started as soon as possible. Four doses of hepatitis B-containing vaccine are permitted when a combination vaccine that includes HBV is used to complete the series following a birth dose. For subsequent doses, careful adherence to minimum age and minimum dose intervals is important. The minimum age to receive the final dose in the series is 24 weeks. The minimum interval needed between dose 1 and 2 is 4 weeks, and the minimum interval between dose 2 and 3 is 8 weeks.

ACIP also recommends catch-up vaccination for all children and adolescents under 19 years of age who have not yet completed the vaccine series. This can be accomplished with a three-dose series of the pediatric formulation of vaccine administered on a 0-, 1-, and 6-month schedule. Adolescents 11–15 years of age also have the option to be immunized with an alternative two-dose regimen using the adult formulation of Recombivax HB, with a minimum interval of 4 months between doses.

Hepatitis B Vaccine Recommendations: Adults

ACIP recommends hepatitis B vaccine for anyone who desires protection from the disease. A stated or identified risk factor is not required. In addition, vaccine is recommended for individuals and groups at high risk for infection who have not previously been immunized (Table 14.1). Identifying and vaccinating high-risk individuals before they become infected can be challenging. Available options for completing standard hepatitis B vaccination regimens in adults are shown in Table 14.2. As a group, individuals being treated with hemodialysis are at high risk for infection with hepatitis B but respond poorly to standard vaccination regimens. For these reasons, the dose and/or schedule used to vaccinate this patient population has been modified. Two options are available. Recombivax HB can be administered as a three-dose series at 0, 1, and 6 months using 40 mcg per dose. Alternatively, Engerix-B can be administered as a four-dose series at 0, 1, 2, and 6 months using 40 mcg per dose. Serologic responses should be monitored, and booster doses given as necessary.

Table 14.1 Individuals and groups recommended to receive hepatitis B vaccine

Underlying medical conditions	Known or high risk for exposure	Social and behavioral risks
Chronic liver disease	Victims of sexual assault or abuse	Individuals who inject drugs and those in drug treatment programs
Chronic hepatitis C infection	Household contacts of individuals with chronic HBV infection	Men who have sex with men, individuals with multiple sexual partners
Kidney disease including those requiring dialysis	Sexual partners of individuals with chronic HBV infection	Residents of correctional facilities
HIV infection, diabetes mellitus, need for solid organ transplantation	Healthcare and public safety workers, those working in correctional facilities	International travel to endemic areas
Individuals requiring treatment with blood products	Residents and staff of facilities for people with developmental disabilities	Individuals seeking evaluation or treatment for a sexually transmitted infection

Table 14.2 Options to complete the hepatitis B vaccination series in adults

Vaccine	Dose	Number of doses	Dosing schedule
Engerix-B	20 mcg in 1 mL	3	0, 1, and 6 mos
Recombivax HB	10 mcg in 1 mL	3	0, 1, and 6 mos
Heplisav-B	20 mcg in 0.5 ml	2	At least 4 weeks apart
Twinrix: Option 1	20 mcg in 1 mL[a]	3	0, 1, and 6 mos
Twinrix: Option 2	20 mcg in 1 mL[a]	4	0, 7 days, 21–30 days, 12 mos

[a]Also contains 720 ELISA units of inactivated hepatitis A

Contraindications to Vaccine

Contraindications to hepatitis B vaccine include a life-threatening allergic reaction following a previous dose or a known severe allergy to any vaccine component including neomycin (Twinrix, Pediarix, Vaxelis), polymyxin B (Pediarix, Vaxelis), and streptomycin sulfate (Vaxelis). Moderately to severely ill individuals should postpone immunization until they have recovered from the acute illness.

Warnings and Precautions for Vaccine Use

Careful consideration should be given to vaccinating a premature infant who has a history of apnea after receiving any vaccination. Syncope and near-syncopal episodes from vasovagal reactions are known to occur following the administration of any injectable vaccine, particularly in the adolescent population. When immunizing with Recombivax HB, Engerix-B, Twinrix, and Pediarix, caution should be used for individuals with a known hypersensitivity to latex.

Side Effects and Adverse Events of Monovalent Hepatitis B Formulations

Transient, mild-to-moderate soreness at the injection site, with or without low-grade fever, lasting up to 2 days is reported frequently. Symptoms associated with vasovagal reactions to the injection, including dizziness, ringing in the ears, and syncope, are seen regularly, particularly among adolescents. Periodic breathing and/or apnea can be seen in premature infants following vaccination. Severe allergic reactions with hives, swelling of the face and throat, and difficulty breathing are very rare occurrences, estimated at 1 per million doses.

Vaccine-Specific Safety Profiles

Mild-to-moderate injection site reactions, including pain, tenderness, pruritus, or erythema, were seen in 17% of healthy children ≤10 years old who received Recombivax HB. Overall, 10.4% experienced systemic adverse reactions. Complaints, in decreasing order of frequency, included irritability, fever >101 °F, diarrhea, fatigue, and loss of appetite. Similarly, immunized adults have reported pain, swelling, and/or bruising at the injection site. 15% experienced systemic symptoms, most commonly as fatigue, malaise, and fever >100 °C.

Engerix-B is also generally well tolerated. The most commonly reported side effects reported from adults and children enrolled across 36 clinical trials were injection site soreness (22%) and fatigue (14%). Other fairly common adverse reactions reported from 1–10% of all vaccinees included injection site erythema, induration and/or swelling, dizziness, and headaches. Fewer than 1% reported chills, influenza-like symptoms, irritability, malaise, weakness, anorexia, rash, and/or minor gastrointestinal complaints.

Local injection site reactions were also commonly reported during clinical trials with Heplisav-B. The most common local reactions included injection site pain (23–39%), redness (1–4%), and swelling (1–2%), while the most common systemic reactions reported were fatigue (11–17%), headache (8–17%), malaise (7–9%), and myalgias (6–9%).

Post-marketing safety surveillance and case-controlled studies indicate that hepatitis B vaccines are safe and well tolerated. They do not cause Guillain-Barre syndrome, chronic fatigue syndrome, rheumatoid arthritis, type 1 diabetes, or other autoimmune diseases. There is no association between HBV vaccination and the development of multiple sclerosis, and vaccination does not increase the short-term risk of relapse in multiple sclerosis. In addition, no causal relationship between hepatitis B vaccination and other neurologic disorders, including leukoencephalitis, optic neuritis, and transverse myelitis, has been identified.

Estimated Vaccine Efficacy from Clinical Vaccine Trials

During convalescence from acute hepatitis B infection, individuals who develop a robust antibody response directed against HBsAg clear the infection. Serum concentrations of anti-HBsAg antibody at or exceeding 10 mIU/mL are known to be seroprotective. Similarly, individuals who are immunized with HBV vaccine, and subsequently shown to have seroprotective concentrations of anti-HBsAg antibody, are considered to be immune to infection. This serologic correlate of immunity allows for straightforward interpretation of immunogenicity results collected during vaccine trials. Given the ongoing high prevalence of infection in many parts of the world, clinical trials to determine vaccine efficacy (i.e., the ability of vaccine to prevent infection) can also be designed.

The protective efficacy of administering both a birth dose of HBIG and a three-dose series of Recombivax to infants born to HBsAg- and HBeAg-positive mothers was shown to be 96%. Recombivax HB is highly immunogenic. Following a three-dose series of the vaccine, 100% of 92 infants, 99% of 129 children, and 99% of 112 adolescents achieved anti-HBsAg antibody concentrations exceeding 10 mIU/mL. The immunogenicity of a two-dose regimen of the adult formulation (10 mcg/1 mL) when administered to 255 adolescents between 11 and 15 years was 99%. Immunogenicity of a three-dose regimen (10 mcg/1 mL) in adults varied by age: 98% of 787 adults 20–29 years old, 94% of 249 adults 30–39 years old, and 89% of 177 adults ≥40 years old achieved protective antibody concentrations. Hemodialysis patients respond less well than healthy adults, even when using the higher 40 mcg/1 mL dose formulation. Seroprotection rates are higher in those vaccinated earlier in disease, especially those who are immunized before they begin hemodialysis.

The efficacy of Engerix-B was evaluated in infants born to mothers positive for both HBsAg and HBeAg without the coadministration of HBIG at birth ($n = 58$). Only two infants became chronic hepatitis carriers during the 12-month follow-up period, giving the vaccine series a protective efficacy rate of 95%. Vaccine efficacy was also evaluated in men who have sex with men ($n = 244$). Four subjects became infected prior to completing the three-dose series. None of those who had completed the three-dose series became infected during the 18-month follow-up period.

Neonates who received a three-dose series of vaccine (10 mcg/0.5 mL) given at 0, 1, and 6 months ($n = 52$) achieved 97% seroprotection. Children aged 6 months to 10 years ($n = 242$) achieved 98% seroprotection, and children aged 5–16 years ($n = 181$) achieved 99.5% seroprotection. Similarly, adolescents aged 11–19 years ($n = 122$) achieved 99% seroprotection, and individuals ≥40 years old ($n = 50$) achieved 88% seroprotection.

Studies of the immunogenicity of a two-dose (20 mcg/0.5 mL) series of Heplisav-B, given 4 weeks apart, showed seroprotective rates across all groups exceeding 90%. Vaccine immunogenicity was seroprotective in 100% of 18- to 29-year-olds ($n = 174$), 98.9% of 30- to 39-year-olds ($n = 632$), 97.2% of 40- to 49-year-olds ($n = 974$), 95.2% of 50- to 59-year-olds ($n = 1439$), and 91.6% of 60- to 70-year-olds.

Seroprotective rates of the hepatitis B component of Twinrix, Pediarix, and Vaxelis were noninferior to their respective monovalent hepatitis B vaccines.

Impact of Vaccine on Disease Burden

In 1990, global hepatitis B vaccine coverage rates were estimated to be 1%. In 1992, the World Health Assembly passed a resolution recommending the inclusion of HBV vaccine in the Expanded Programme on Immunization by 1997. Efforts were successful worldwide. By 2014, global coverage rates with three doses of hepatitis B vaccine had increased to an estimated 82% with regional coverage as high as 92% in the Western Pacific. Between 1992 and 2015, the number of countries in the world routinely vaccinating infants with hepatitis B vaccine increased from 31 to 185. In 2015, 84% of children had received a three-dose series, but only 39% of newborns received a birth dose. The African, Eastern Mediterranean, and European regions all remain below the global average.

Hepatitis B vaccines are safe and highly effective at preventing infection and its associated complications. Globally, vaccine uptake exceeds 80% with some regions reporting vaccination rates of 93% or more.

References and Suggested Reading

World Health Organization

https://www.who.int/news-room/fact-sheets/detail/hepatitis-b

Vaccine Information Sheets

https://www.cdc.gov/vaccines/hcp/vis/vis-statements/hep-b.html,

Recombivax HB Package Insert

https://www.fda.gov/media/74274/download

Engerix-B Package Insert

https://www.fda.gov/media/79341/download

Heplisav-B Package Insert

https://www.fda.gov/media/108745/download

Twinrix Package Insert

https://www.fda.gov/media/74182/download

Pediarix Package Insert

https://www.fda.gov/media/79830/download

Vaxelis Package Insert

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