8 Hepatitis B

Key information

Mode of transmission	Contact with infected blood or body fluids during childbirth (vertical transmission); sexual intercourse, intravenous drug use, or contact with broken skin (horizontal transmission).
Incubation period	45–180 days, commonly 60–90 days.
Period of communicability	Potentially infectious 2–3 weeks before the onset of symptoms, during the clinical disease and usually for 2–3 months after acute hepatitis B illness; as long as HBsAg continues to be present in blood.
Burden of disease	New Zealand is a country with a low overall prevalence of hepatitis B carriage, but it contains certain populations with high prevalence. All pregnant women and high-risk groups should be screened for chronic infection. HBV acquisition in infancy is very likely to lead to chronic infection. Chronic HBV infection can progress to cirrhosis and liver cancer.
Funded vaccines	HepB (HBvaxPRO). DTaP-IPV-HepB/Hib (Infanrix-hexa).
Dose, presentation, route	HepB: • 5 µg presentation – 0.5 mL per dose • 10 and 40 µg presentations – 1.0 mL per dose • single dose vial. DTaP-IPV-HepB/Hib: • 0.5 mL per dose • pre-filled syringe and glass vial – the vaccine must be reconstituted prior to injection. Intramuscular injection.

Continued overleaf

Funded vaccine indications and schedule	At ages 6 weeks, 3 months and 5 months: DTaP-IPV-HepB/Hib. Babies born to HBsAg-positive mothers should receive HepB vaccine plus HBIG at birth, then the usual childhood schedule. Serological testing (anti-HBs and HBsAg) at age 9 months. Individuals with eligible conditions: HepB (see section 8.5).
Vaccine efficacy/ effectiveness	In general, efficacy is 85–95 percent, though likely to be lower in older individuals and those with immunocompromise. Protection is expected to be lifelong. Boosters are not recommended.

8.1 Virology

The hepatitis B virus (HBV) is a partially double-stranded DNA virus belonging to the Hepadnaviridae family. Three major subunits make up the structural components:

- the HBV genome, a small, circular, partially double-stranded DNA molecule, in association with a polymerase enzyme
- the nucleocapsid core, which surrounds the genome and consists of core protein (hepatitis B core antigen, HBcAg)
- the outer lipoprotein envelope, which contains the hepatitis B surface antigen (HBsAg).

The genome has four genes (S, C, X and P). Both the core nucleocapsid protein (HBcAg) and the 'early' protein (which makes HBeAg) are translated from the C gene. HBcAg is essential for viral packaging and is an integral part of the nucleocapsid. HBeAg is a soluble protein that is not part of the virus particle. Detection of HBeAg in the serum is correlated with viral replication, and is most commonly found in those with acute hepatitis B and those with chronic HBV infection with high viral load.[1]

8.2 Clinical features

There is a broad spectrum of clinical disease with HBV infection, from subclinical through to fulminant hepatitis. Persistent infection can lead to chronic liver disease, potentially causing cirrhosis or hepatocellular carcinoma.

8.2.1 Serological markers of infection

The HBV antigens and their associated antibodies are serological markers of HBV infection or vaccination (Table 8.1). At least one serological marker is present during the different phases of infection (Table 8.2).

Table 8.1: HBV antigens and their respective antibodies

Antigen	Antibody
HBsAg (hepatitis B surface antigen)	Anti-HBs (antibody to HBsAg), (IgM, IgG, and total)
HBcAg (hepatitis B core antigen)	Anti-HBc (antibody to HBcAg), (IgM, IgG and total)
HBeAg (hepatitis B e antigen)	Anti-HBe (antibody to HBeAg), (IgM, IgG and total)

Table 8.2: Interpretation of serology for HBV infection

Serological marker				Interpretation
HBsAg	Total anti-HBc	IgM anti-HBc	Anti-HBs	
–	–	–	–	Never infected
+	+	+	–	Acute infection
–	+	+	+ or –	Acute resolving infection
–	+	–	+	Recovered from past infection and is immune
+	+	–	–	Chronic infection[a]
–	–	–	+	Immune if ≥10 IU/L.[b] Vaccinated or natural infection.

Key: Anti-HBc = antibody to hepatitis B core antigen; anti-HBs = antibody to hepatitis B surface antigen (HBsAg); IgM = immunoglobulin M; + = positive test result; – = negative test result.

a HBeAg positive (HBeAg+) correlates with high viral load and increased risk of transmission; HBeAg negative (HBeAg–) correlates with lower viral load and reduced risk of developing cirrhosis or cancer.

b Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.

Adapted from: Van Damme P, Ward J, Shouval D, et al. 2013. Hepatitis B vaccines. In: Plotkin SA, Orenstein WA, Offit PA (eds). *Vaccines* (6th edition). Philadelphia, PA: Elsevier Saunders. Table 15.1.

See the 'Hepatitis B' chapter of the *Communicable Disease Control Manual 2012*[2] for recommendations for HBV case and contact management.

8.2.2 Acute hepatitis

The virus preferentially infects liver cells, multiplying there and releasing large amounts of HBsAg, which is present in the blood of people with active infection. The incubation period varies between 45 and 180 days, and is commonly 60 to 90 days.

HBV is not directly cytopathic; it is the host's immune response that leads to death of the infected liver cell. Most infected people mount an effective immune response that leads to eradication of infection over a period of several months. Adults with acute infection may be asymptomatic (approximately 20 percent) or have symptomatic hepatitis (approximately 80 percent, but these proportions vary[3]).

The common symptoms of acute hepatitis B illness are fever, jaundice, malaise, anorexia, nausea, vomiting, myalgia and abdominal pain. Jaundice usually develops within two weeks of onset of the illness, and dark urine and/or clay coloured stools might appear up to five days before clinical jaundice. Clinical signs and symptoms of acute hepatitis B usually resolve one to three months later.[1]

There is a small risk of liver failure (less than 1 percent) with acute infection; almost half will die or require emergency liver transplantation.

8.2.3 Chronic HBV infection

The main burden of HBV disease occurs in people with chronic HBV infection. Chronically infected people are identified by presence and persistence of HBsAg in their serum for at least six months. The age of acquisition of HBV is strongly associated with the risk of developing chronic HBV infection. Approximately 90 percent of those infected perinatally or in infancy develop chronic HBV infection, compared with 30 percent of children infected between ages 1 and 4 years and less than 5 percent of people infected as adults.

Infants seldom mount an immune response to HBV infection, and infection in infancy is often asymptomatic. Asymptomatic chronic infection stimulates persistent immune responses that may eventually lead to cirrhosis (decades later); cirrhosis and chronic infection increase the risk of development of hepatocellular carcinoma.

Chronically infected people who are HBsAg positive can also have HBeAg detectable in the serum, and this combination is considered most infectious. Although recent evidence suggests HBeAg negative patients are less infectious, it is dependent on HBV DNA levels. Whatever the case, both groups can be an ongoing source of infection to susceptible individuals. In the early years of chronic infection, high rates of viral replication are common, and both HBeAg and high levels of HBV DNA are present in the blood. In later years, HBeAg may be absent from the blood, and HBV DNA levels are usually lower, both of which correspond with lower rates of viral replication.

8.2.4 Routes of transmission

HBV is usually transmitted through contact with infected blood or body fluids during childbirth, contact with broken skin, or during sexual intercourse or intravenous drug use. Although HBV can be found in all body fluids, blood has the highest concentration and saliva the lowest. HBV in dried blood remains infective for at least one week.[4]

Perinatal (vertical) transmission

The primary source of HBV infection is perinatal exposure from mothers with chronic HBV infection. Transmission usually occurs at the time of birth. The *in utero* transmission of HBV is relatively rare,[5] accounting for less than 2 percent of infections transmitted from mother to infant.

If no prophylaxis is given to the infant, the baby of an HBeAg positive mother has a 70–90 percent risk of infection, while the baby of an HBeAg negative, HBsAg positive carrier mother has a 5–20 percent risk of infection. Over 90 percent of infants who acquire infection perinatally go on to become chronic carriers.

Person-to-person (horizontal) transmission

Non-sexual person-to-person transmission probably occurs from inadvertent percutaneous or mucosal contact with blood or infectious body fluids amongst people in close daily contact (household members).

The main sources of transmission are:

- sexual contact with an infected individual
- percutaneous exposure to blood or infectious body fluids
- needle-stick injuries or sharing needles
- travelling to high endemic countries (see below).

8.3 Epidemiology

8.3.1 Global burden of disease

Approximately two billion people have been exposed to HBV, and an estimated 240 million people have chronic infection and remain at risk of developing cirrhosis and hepatocellular carcinoma.[6, 7] More than 90 percent of individuals with chronic HBV reside in the Asia–Pacific region, where most countries have high prevalence rates of HBV infection (the population rate of HBsAg positivity is between 5 and 20 percent). More than 99 percent of HBV-infected people in this region acquired infection through vertical transmission from their mother (usually at the time of delivery) or in early childhood. Acquisition of HBV during adulthood (usually via sexual transmission or injecting drug use) is associated with a high rate of symptomatic hepatitis but a low rate of chronic infection.

The introduction of universal childhood HBV immunisation has changed the epidemiology of chronic infection in many countries, but it will be several decades (one to two human generations) before the full benefits are realised. The world can be divided into regions with high (8 percent and over), high-intermediate (5–7 percent), low-intermediate (2–4 percent) and low (less than 2 percent) prevalence of chronic infection, defined as the presence of HBsAg in serum.[8, 9]

In regions with a high prevalence of chronic infection, the lifetime risk of exposure to HBV is almost 80 percent, with most infections occurring in the first decade of life. The Pacific Islands and most of Asia (except Japan and India) are high-prevalence regions. Other high-prevalence regions include Sub-Saharan Africa and Latin America.[8] In contrast, in countries with a low HBsAg prevalence, the lifetime risk of HBV exposure is less than 20 percent, with most infections acquired in adulthood.

New Zealand has a low overall prevalence of hepatitis B carriage but contains certain populations with high prevalence (see section 8.3.2 below).

8.3.2 New Zealand epidemiology

Before the introduction of HBV immunisation in New Zealand, HBV transmission was common among preschool and school-aged children. The exact mode of transmission is uncertain but is thought to be related to close contact. In the eastern Bay of Plenty region almost half of the population were infected by age 15 years.[10, 11] Even after the introduction of universal HepB in 1988 (see Appendix 1), there were regions in New Zealand where children were still at risk of HBV infection due to poor immunisation coverage rates.[12, 13, 14]

Acute HBV infection

Only acute hepatitis B is a notifiable disease in New Zealand. Therefore notification rates do not describe the burden of chronic HBV infections.

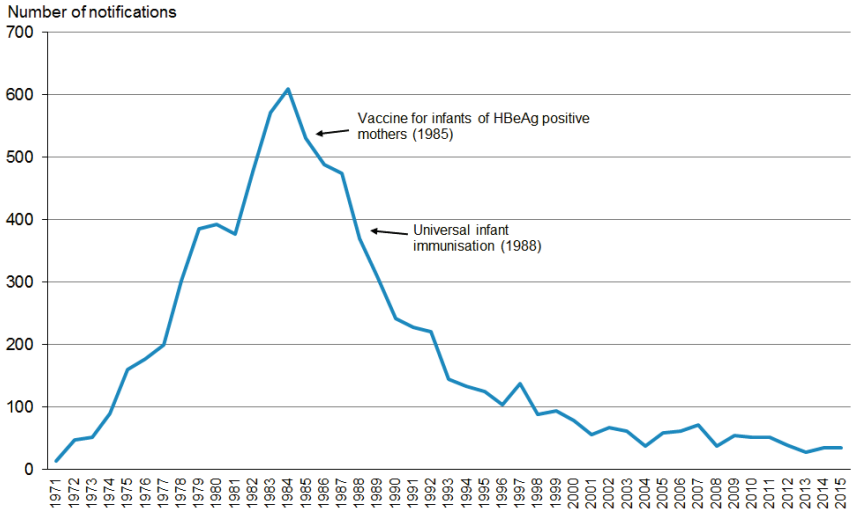
The HBV notification rate in 2015 was 0.7 per 100,000 population (34 cases), similar to the 2014 rate (0.8 per 100,000, 35 cases).[15] The highest notification rate was in the 40–49 and 50–59 years age groups (both 1.3 per 100,000). The notification rate was higher for males (1.1 per 100,000 population) than for females (0.4 per 100,000).

Ethnicity was recorded for 32 cases (94.1 percent).[15] The Māori (0.9 per 100,000) and European/Other (0.6 per 100,000) ethnic groups had the highest hepatitis B notification rates.

The most common risk factors reported in 2015 were overseas travel and sexual contact with a confirmed case or person with chronic HBV infection.

Hepatitis B notifications have declined from 609 cases in 1984 to 34 cases in 2015 (see Figure 8.1). While difficult to quantify accurately, the introduction of universal infant immunisation in 1988 has contributed to the dramatic decline in the number of newly notified cases of HBV infection.

Figure 8.1: Notifications of hepatitis B, 1971–2015



Source: Ministry of Health and ESR

Chronic HBV infection

Approximately 100,000 people in New Zealand are chronically infected with HBV. The National Hepatitis B Screening Programme was a three-year programme that started in 1999 and targeted at-risk populations in the North Island (Māori, Pacific peoples and Asian New Zealanders aged over 15 years). The programme also enrolled people from other ethnic groups and included follow-up of individuals aged under 15 years with chronic HBV.

Approximately one-third of the at-risk populations were screened. Of these, the highest rates were among Chinese (9.1 percent), Pacific peoples (8.5 percent) and Māori (5.8 percent). Although Europeans were not specifically targeted in this screening programme, they have an estimated prevalence rate of 1 percent (higher than in Australia, North

America and Europe), reflecting increased risk of childhood horizontal transmission.[16]

A New Zealand-based modelling study estimated that until the year 2100, people with chronic HBV infection will continue to provide a source of infection to susceptible people.[17] Increased immigration from high-prevalence countries in the Asia–Pacific region is also likely to influence HBV prevalence in New Zealand.

Because people who acquire chronic HBV infection in childhood usually do not develop hepatocellular carcinoma until aged 40 years or older, the introduction of a universal HBV vaccination in 1988 is unlikely to have a significant effect on the incidence of hepatocellular carcinoma until approximately 2030.

A retrospective laboratory data study of antenatal HBsAg tests from the Midlands region (Bay of Plenty, Eastern Bay of Plenty, Waikato and Rotorua) between 1997 and 2009 found a declining prevalence of HBV infection. This decrease was seen across all age groups, but was most marked in the antenatal tests of women aged under 20 years, due to receipt of funded HepB in childhood.[18]

A recent long-term follow-up study in New Zealand has shown horizontally acquired HBV infection during childhood in Māori and Pacific peoples correlates with increased rates of hepatocellular carcinoma and liver-related mortality.[19] This study emphasises the importance of early protection of the infant with vaccination.

Strategy for prevention

In 1988 New Zealand was one of the first countries to introduce universal infant hepatitis B immunisation. At the end of 2016 approximately 93 percent of New Zealand children aged 2 years had completed a primary course of HepB, which confers lifelong immunity in approximately 95 percent of vaccinees.

8.4 Vaccines

8.4.1 Available vaccines

A number of HBV-specific monovalent and combination vaccines that contain recombinant HBsAg (HepB) are licensed (approved for use) and available (marketed) in New Zealand.

Funded vaccines

- HepB (HBvaxPRO, MSD): contains either 5 µg, 10 µg or 40 µg of HBsAg per dose; it does not contain a preservative. Other components and residuals include amorphous aluminium hydroxysulphate, sodium borate, sodium chloride and yeast (less than 1 percent of the protein content is from yeast).
- DTaP-IPV-HepB/Hib (Infanrix-hexa, GSK): diphtheria, tetanus, acellular pertussis, inactivated polio, hepatitis B and *Haemophilus influenzae* type b vaccine (see section 5.4.1 for more information).

Other vaccines

- HepB: Engerix-B (GSK)
- HAV-HepB (hepatitis A and hepatitis B vaccine): Twinrix and Twinrix Junior (GSK) (see also section 7.4.1).

8.4.2 Efficacy and effectiveness

See also section 14.4.2 for information about the DTaP-IPV-HepB/Hib vaccine.

Immunogenicity

Clinical trials in high-risk groups have shown a vaccine efficacy of 85–95 percent. Serum anti-HBs antibody ≥10 IU/L is the WHO measure of immunity and is considered a correlate of protection. In the primary care setting, individuals who have had a documented seroconversion after three injections are expected to have lifelong

immunity with no need for further boosters, even if circulating antibody is subsequently not detectable.

Smoking, obesity, HIV infection and chronic disease (including renal failure) all reduce vaccine efficacy, but age is the primary factor affecting the response. At least 98 percent of infants, 95 percent of children and 90 percent of adolescents develop protective levels of antibody after three doses of vaccine. Some non-responders to the initial vaccination course will not produce adequate antibody levels. These people should be offered a full second course of three injections.

However, some people are persistent non-responders. Persistent non-responders often have an impaired immune system, such as organ transplant recipients and those with HIV infection or chronic disease, including advanced cirrhosis, renal failure or those undergoing haemodialysis (see section 8.5.7).

For babies of HBeAg-positive mothers, controlled trials have shown that vaccine at birth provides 75 percent protection from infection, while administration of HBIG in addition to vaccination provides 85–95 percent protection against transmission.[1, 20] Protection is reduced to less than 80 percent when the mother's HBV DNA level is greater than 10^8 IU/mL (or 10^8 copies/mL). In this situation, administration of tenofovir (an antiviral agent) to the mother during the last trimester is recommended and funded.

Duration of immunity

The development of anti-HBs antibodies after a primary vaccination course (three injections and seroconversion) indicates development of immune memory. The quantity of antibody in serum is thought to determine the length of time the antibody titre can be detected in the blood, although any reading ≥10 IU/L post-vaccination course is considered protective. Once a seroprotective level is reached after the three-dose primary vaccination course, booster doses of vaccine are unnecessary.[21, 22] Children who are given booster doses up to 12 years after the primary series show strong anamnestic (secondary) responses, indicating the boost was unnecessary.

There is evidence from Taiwan,[23] Alaska[24] and Hawaii[25] that boosters of HepB are unnecessary following completion of infant immunisation. This is despite the fact that a large proportion of vaccinees will lose detectable antibodies within seven years of vaccination. Long-term protection from clinical infection despite loss of neutralising antibody is thought to reflect a strong cellular memory immune response following HBV vaccination. Vaccinees who are subsequently infected with HBV do not develop clinical illness but may have anti-HBc present in plasma.

Effects on chronic HBV infection

In all populations where it has been measured, immunisation has led to a dramatic drop in HBV chronic infection.[26] For example, chronic HBV infection dropped from 16 percent to zero in Alaska as a result of 96 percent immunisation coverage. In Taiwan, the incidence of hepatocellular carcinoma also decreased in children as a result of the immunisation programme.[27, 28]

8.4.3 Transport, storage and handling

Transport hepatitis B vaccines according to the *National Standards for Vaccine Storage and Transportation for Immunisation Providers 2017*.[29] Store at +2°C to +8°C. Do not freeze.

DTaP-IPV-HepB/Hib should be stored in the dark.

DTaP-IPV-HepB/Hib (Infanrix-hexa) must be reconstituted by adding the entire contents of the supplied container of the DTaP-IPV-HepB vaccine to the vial containing the Hib pellet. After adding the vaccine to the pellet, the mixture should be shaken until the pellet is completely dissolved. Use the reconstituted vaccine as soon as possible. If storage is necessary, the reconstituted vaccine may be kept for up to eight hours at 21°C.

8.4.4 Dosage and administration

Each 0.5 mL dose of DTaP-IPV-HepB/Hib (Infanrix-hexa) vaccine contains 10 µg of HBsAg, and is administered by intramuscular injection (see section 2.2.3).

The dose of HepB vaccine (5 µg HBsAg per 0.5 mL, 10 µg per 1.0 mL or 40 µg per 1.0 mL) varies according to the age of the individual and/or their health status. HepB vaccine is administered by intramuscular injection.

Co-administration with other vaccines

Hepatitis B vaccines may be given at the same time as all other vaccines on the Schedule, including measles, mumps and rubella (MMR) vaccine.

If a course of vaccine is interrupted, it may be resumed without repeating prior doses (see Appendix 2).

8.5 Recommended immunisation schedule

Table 8.3: Hepatitis B vaccine recommendations, funded and unfunded

Note: Funded conditions are in the shaded rows. See the Pharmaceutical Schedule (www.pharmac.govt.nz) for any changes to the funding decisions.

Recommended and funded
Household or sexual contacts of HBsAg-positive patients (ie, patients with acute or chronic HBV infection)
Babies of HBsAg-positive mothers (ie, mothers with acute or chronic HBV infection) – require a birth dose plus the primary series (HBIG is also given to these babies at birth)
Children and adolescents aged under 18 years who are considered not to have achieved a positive serology and require additional vaccination or require a primary course of vaccination
HIV-positive patients[a]
Hepatitis C-positive patients[b]
Following non-consensual sexual intercourse
Following immunosuppression[a,c]
Solid organ transplant patients[a]
Post-HSCT patients[a]
Following needle-stick injury
Dialysis patients[a,d]
Liver or kidney transplant patients[a,d]

Continued overleaf

Recommended, not funded
Adults at occupational risk (see section 4.6)
Adults at risk of infection by sexual exposure: • people seeking evaluation or treatment for a sexually transmitted infection • people with a high number of sexual partners • people who have sex with commercial sex workers • men who have sex with men
Individuals with haemophilia and other regular recipients of blood products
Prison inmates
Current or recent injecting drug users
Migrants from HBV endemic countries (HBsAg prevalence ≥2%)[e]
Individuals with developmental disabilities
Travellers to HBV endemic regions (HBsAg prevalence ≥2%)[e]

a See also section 4.3.3

b Hepatitis C patients should also receive hepatitis A vaccine, although this is not currently funded.

c The period of immunosuppression due to steroid or other immunosuppressive therapy must be longer than 28 days.

d The 40 µg dose of HepB is recommended for adult dialysis patients or for adult liver or kidney transplant patients. See Table 8.5.

e See the Centers for Disease Control and Prevention website for countries with HBsAg prevalence ≥2% (wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/hepatitis-b). Consider combined Hep A and B vaccination for travellers to these regions.

8.5.1 Usual childhood schedule

A primary course of hepatitis B vaccination is given as three doses of DTaP-IPV-HepB/Hib at ages 6 weeks, 3 months and 5 months (Table 8.4). If a course of immunisation is interrupted for any reason, it may be resumed without repeating prior doses (see section 8.5.3 and Appendix 2).

Table 8.4: Usual childhood schedule for hepatitis B-containing vaccine (excluding catch-up)

Age	Vaccine	Comment
6 weeks	DTaP-IPV-HepB/Hib	Primary series
3 months	DTaP-IPV-HepB/Hib	Primary series
5 months	DTaP-IPV-HepB/Hib	Primary series

Preterm infants of HBsAg-negative women

Some low birthweight or preterm infants may have a reduced response to HepB at birth.[30] However, by the chronological age of 1 month, all medically stable preterm infants, regardless of initial birthweight or gestational age, respond to HepB as well as term and larger infants.[31] Because New Zealand's Schedule starts at age 6 weeks, low birthweight and preterm infants are expected to respond to HepB. (See also section 4.2.1.)

Infants with liver or renal disease

HepB vaccine is funded for liver or kidney transplant patients and for dialysis patients. For infants requiring transplants, see section 4.2.3. For infants undergoing dialysis, see 'Chronic kidney disease (CKD)' in section 4.3.3.

8.5.2 Babies born to HBsAg-positive mothers

The routine schedule for these infants is a birth dose of 5 µg of HepB plus HBIG, then three doses of hepatitis B (as DTaP-IPV-HepB/Hib) at ages 6 weeks, 3 months and 5 months.

All pregnant women should receive antenatal screening for hepatitis B infection by testing for HBsAg. Babies of HBsAg-positive mothers are to be notified at birth using the form *HE1446: Consent for hepatitis B vaccine and hepatitis B immunoglobulin and notification to the Medical Officer of Health*, available from www.healthed.govt.nz or the local authorised health education resource provider or public health unit.

Babies born to HBsAg-positive mothers should receive:

- 100–110 IU HBIG neonatal, at or as close as possible to birth
- a birth dose of HepB (HBvaxPRO, 5 μg), which should be given at or as close as possible to birth (preferably within 12 hours).

If HBIG and/or HepB is inadvertently omitted, administer as soon as the omission is recognised. HBIG can be administered up to seven days post-delivery. If there is a delay for longer than seven days, seek specialist advice.

These babies should then continue as per the Schedule at ages 6 weeks, 3 months and 5 months. Serological testing is required at 9 months of age (see below).

The vitamin K injection may also be given at the same time, in the same limb as the HBIG, but not at the same site.

Occasionally women have not been tested for their HBsAg status during the antenatal period. If a woman's HBsAg status is unknown at the time of delivery, the baby should be given HepB at the time of delivery while waiting for the result of an urgent HBsAg test on the mother. If she is found to be HBsAg positive, the baby should be given HBIG as soon as possible, up to seven days post-delivery.[31] Subsequent vaccine doses are given as per the Schedule.

It is essential to take blood to determine whether the baby has seroconverted (anti-HBs positive) or has become infected despite immunoprophylaxis (HBsAg positive), or is neither infected nor immune (ie, HBsAg negative and anti-HBs negative). Testing should not be performed before 9 months of age to avoid detection of anti-HBs from HBIG administered during infancy and to maximise the likelihood of detecting late HBV infections.[31]

Babies of HBsAg-positive mothers should be placed on a practice recall system to have their blood tested at 9 months of age, and should be rechecked at the 15-month immunisation event to ensure that testing has occurred. The serology results should be interpreted as in Figure 8.2.

Figure 8.2: Management of a baby of an HBsAg-positive woman

Screen all women in early pregnancy for hepatitis B carriage

Woman is HBsAg positive **No** → See section 8.5.1: 'Usual childhood schedule'

Yes ↓

All HBsAg-positive pregnant women should also be tested for HBeAg and should have HBV DNA measured. The results should be discussed with a specialist or the woman should immediately be referred to a specialist for ongoing care.

Give the baby hepatitis B protection as follows.

At age	Action to be taken
Birth	Give HBIG 100–110 IU **and** HepB 5 µg
6 weeks	DTaP-IPV-HepB/Hib
3 months	DTaP-IPV-HepB/Hib
5 months	DTaP-IPV-HepB/Hib
9 months	Take a blood test to check for hepatitis B infection (HBsAg) and for vaccine-induced immunity (anti-HBs). • If HBsAg is negative and anti-HBs level is ≥10 IU/L* at age 9 months, immunity is proven. • If HBsAg is positive, the baby has become infected despite prophylaxis: refer to an appropriate specialist. If HBsAg is negative and anti-HBs level is <10 IU/L* at age 9 months, give a further 3 doses of HepB at least 4 weeks apart. Recheck serology 4 weeks after the last dose. If there is no seroconversion after the third further dose of HepB (ie, if anti-HBs is still <10 IU/L*), discuss with a specialist.

All other vaccines should be administered as per the Schedule.

* Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.

Neonatal HBIG plus vaccine will fail to prevent vertical HBV transmission in more than 20 percent of infants born to HBsAg-positive mothers with serum HBV DNA levels greater than 10^8 IU/mL (or 10^8 copies/mL). These mothers are usually young, with normal alanine transaminase, and are HBeAg positive. If the mother's HBV DNA level is greater than 10^8 IU/mL, administration of tenofovir (an antiviral agent) during the last trimester is recommended and funded.

The number of such high-risk pregnancies appears to be increasing in this country as a result of the immigration of young Asian women of childbearing age, of whom approximately 8 percent are HBsAg positive, with the majority of those also HBeAg positive. In contrast, the number of HBsAg-positive Māori and Pacific women of childbearing age has decreased markedly due to infant vaccination. In addition, most HBsAg-positive Māori and Pacific women are HBeAg negative, with lower HBV DNA levels (below 10^8 IU/mL).

Babies born to mothers who received oral antiviral therapy for chronic HBV must still receive the recommended neonatal HBIG/vaccine schedule. All other vaccines are administered as per the Schedule.

See Appendix 6 and section 8.8.1 for more information about passive immunisation and HBIG.

Preterm and low birthweight infants of HBsAg-positive women

Preterm and low birthweight infants of HBsAg-positive women should be managed as above, regardless of birthweight or gestation.

8.5.3 Catch-ups for children and adolescents

HepB is recommended and funded for everyone aged under 18 years. If the HepB is not given during the first year of life, three doses of vaccine are recommended. An accelerated two-dose regimen for adolescents aged 11–15 years has been shown to be effective and to improve compliance in this age group. See Appendix 2 for catch-up schedules.

Children and adolescents with liver or kidney disease

HepB vaccine is funded for liver or kidney transplant patients (recommend six months post-transplant) and for dialysis patients.

See Figures 8.3 and 8.4 for serological testing and vaccination recommendations. If non-immune, children aged under 16 years should receive three doses of 10 μg HepB (at 0, 1 and 6 months), those aged 16 years and older should receive three doses of 40 μg HepB. If there is an inadequate immune response to the initial three-dose HepB series (see Figure 8.4), give a further three doses (10 μg or 40 μg, as appropriate).

See also 'Chronic kidney disease (CKD)' and 'Solid organ transplants' in section 4.3.3.

8.5.4 Eligible adults aged 18 years and older

Table 8.5: Hepatitis B vaccine schedules for eligible adults aged 18 years and older

Who	Vaccine	Dose	Volume (mL)	Number of doses	Schedule
Dialysis patients, liver or kidney transplant patients	HepB	40 µg	1.0	3	0, 1, and 6 months*
HIV patients	HepB	10 µg	1.0	4	0, 1, 2, and 12 months
Other eligible adults (see Table 8.3)	HepB	10 µg	1.0	3	0, 1, and 6 months*

* Check the manufacturer's data sheet for accelerated immunisation schedules.

Adult dialysis or adult liver or kidney transplant patients

These adults may have a reduced response to HepB,[32] so the higher-dose (40 µg) formulation is recommended and funded. See section 8.5.7 for information about post-vaccination serology.

(See also 'Solid organ transplants' in section 4.3.3.)

Adult HIV patients

Adult HIV patients should receive four doses of HepB (10 µg) at 0, 1, 2 and 12 months.

(See also 'HIV infection' in section 4.3.3.)

Other eligible adults

Three doses of 10 µg HepB given at 0, 1 and 6 months are recommended. Shorter intervals between the second and third doses lead to lower antibody levels but equivalent seroconversion and therefore provide adequate protection. In healthy adults, a two-dose schedule separated by six months,[33] a three-dose schedule given over three weeks,[34] and various other accelerated schedules have led to

seroconversion rates equivalent to those obtained when following the usual recommended schedule. In general, three doses separated by four-week intervals are recommended, but the doses may be delivered at weekly intervals if more rapid protection is needed.

8.5.5 Pregnancy and breastfeeding

HepB may be given during pregnancy and while breastfeeding. Acute HBV infection in pregnant women may result in severe acute hepatitis for the mother, with associated increased risk of fetal loss or neonatal infection. Vaccination should not be withheld from a susceptible pregnant woman at increased risk of acquiring hepatitis B (eg, the sexual partner of an injecting drug user, or known infected male).

8.5.6 (Re-)vaccination

Hepatitis B-containing vaccines are funded for (re-)vaccination of eligible children, as follows. See also sections 4.2 and 4.3.

DTaP-IPV-HepB/Hib (Infanrix-hexa)

An additional four doses (as appropriate) of DTaP-IPV-HepB/Hib are funded for (re-)vaccination of children aged under 10 years:

- post-HSCT or chemotherapy
- pre- or post-splenectomy
- pre- or post-solid organ transplant
- undergoing renal dialysis
- with other severely immunosuppressive regimens.

Up to five doses of DTaP-IPV-HepB/Hib are funded for children aged under 10 years receiving solid organ transplantation.

HepB (HBvaxPRO)

HepB is funded for children aged under 18 years who are considered not to have achieved a positive serology and require additional vaccination.

8.5.7 Serological testing

- Globally, pre-vaccination serological testing is NOT recommended as a routine practice in primary care.
- The vast majority of people with documented evidence of three HepB injections will be immune where there is low risk of disease.
- Infants born to HBsAg-positive mothers and some individuals who require protection in relation to their employment, eg, health care professionals, require post-vaccination serology.

Screening for chronic infection

Screening for the antigen (HBsAg) is useful where there is increased likelihood of the individual already being infected.

The Hepatitis Foundation of New Zealand[35] recommends that the following individuals are most at risk of HBV – people who:

- are over age 25 years and of Māori, Pacific or Asian ethnicity
- were born outside of New Zealand (eg, refugees)
- have a mother or a close family member who has HBV infection
- live with someone who has HBV
- have had unprotected sexual contact with an HBV-infected person
- have ever injected drugs
- have received a tattoo using unsterile equipment.

Screening for HBsAg is also part of routine antenatal care (see section 8.5.2).

All HBsAg-positive individuals should be offered follow-up under the Hepatitis Foundation Hepatitis B Follow-up Programme to enable early diagnosis and treatment of the complications of severe liver disease and hepatocellular carcinoma. Vaccination is recommended (and funded) for household or sexual contacts of HBsAg-positive people (ie, contacts of people with acute or chronic HBV infection).

Serological testing for high-risk groups

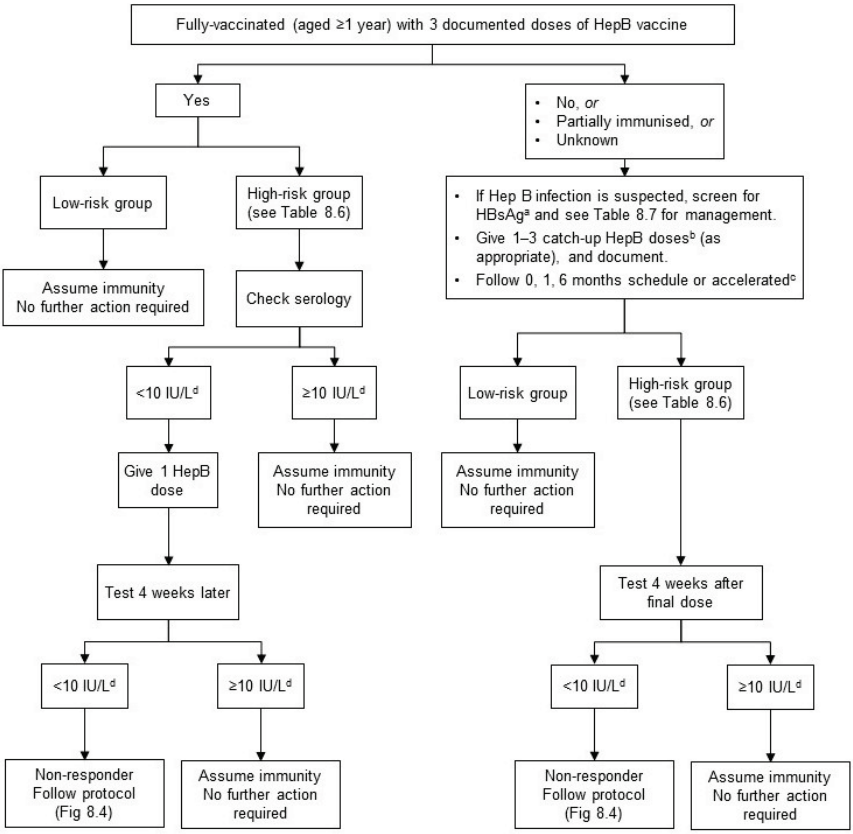
Serological testing is only indicated in high-risk groups (see Table 8.6). These high-risk groups are at higher risk of exposure to HBV, at higher risk of having severe disease or are more susceptible to disease. A flow diagram (Figure 8.3) is included to assist in deciding whether pre- and/or post-vaccination serological testing is indicated. Figure 8.3 may be used for any individual aged 12 months or older, such as for the management of blood and body fluid exposures, or when an adult presents to primary care.

Table 8.6: Individuals at high-risk of hepatitis B infection, for whom serological testing is indicated

Household or sexual contacts of HBsAg-positive patients (ie, patients with acute or chronic HBV infection)
Current or recent injecting drug users
Individuals who change sexual partners frequently (eg, sex workers)
Immunocompromised individuals, including HIV-positive patients
Following non-consensual sexual intercourse
Individuals on immunosuppressive therapies for 28 days or more
Solid organ and post-HSCT patients
Following percutaneous injury (eg, needle-stick injury)
Adults at occupational risk (see section 4.6)
Individuals with haemophilia and other regular recipients of blood products
Inmates of custodial institutions
Individuals with developmental disabilities
People with chronic disease (eg, chronic renal failure requiring haemodialysis, or chronic liver disease)
Migrants from HBV endemic regions (HBsAg prevalence ≥2%)*

* See the Centers for Disease Control and Prevention website for countries with HBsAg prevalence ≥2% (wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/hepatitis-b). Consider combined Hep A and B vaccination for travellers to these regions.

Figure 8.3: Flow diagram for serological testing for hepatitis B



a HBIG may be recommended for non-immune individuals. See Table 8.7.

b Do not count any birth doses of HepB vaccine. See Table 8.3 for the list of funded conditions for HepB vaccine.

c See the manufacturer's data sheet for accelerated HepB schedules.

d Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.

The non-responder protocol

Most vaccinees will develop a high anti-HBs titre, usually greater than 100 IU/L, which usually wanes over time.

Fully vaccinated individuals (ie, three documented doses of HepB) who have at any time had anti-HBs ≥10 IU/L do not need any booster doses, even if antibodies subsequently wane to undetectable levels, which occurs in most individuals by seven years after the last vaccination. If exposed, they will have a secondary anamnestic immune response that will prevent replication of the virus.[1, 36] (Note: Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.)

If a high-risk individual does not achieve a titre of ≥10 IU/L, they should be considered a non-responder and follow the non-responder protocol (Figure 8.4).

Figure 8.4: The non-responder protocol

Individual is high-risk (see Table 8.6), has received three documented doses of HepB and has an anti-HBs <10 IU/L:*

- Complete a second course of three HepB vaccine doses.
- Repeat the serology four weeks after the final HepB vaccine dose.
- If anti-HBs ≥10 IU/L,* then assume immunity. No further action required.
- If, after the second course of three HepB vaccines, they have not achieved anti-HBs ≥10 IU/L,* they should be considered a persistent non-responder to vaccination.
- There is evidence that using a double dose of HAV-HepB (Twinrix) at 0, 1 and 6 months can correct this hyporesponsiveness, using the bystander carrier effect of the HAV component,[37] but this is not funded.
- Persistent non-responders with no immunocompromise who have completed the primary series and a full second course of three vaccine doses should be monitored for wild-type disease, but literature reports of vaccine failures are rare. They should be considered 'unprotected' against hepatitis B and advised to minimise the chance of exposures. Parenteral or mucosal exposure to HBV requires HBIG within 72 hours.

* Some laboratories may require a higher anti-HBs antibody level for proof of immunity. Please follow the testing laboratory's interpretative comments.

Intradermal injections to correct this hyporesponsiveness that have been used in the past, but they are technically difficult and not recommended.

8.6 Contraindications and precautions

See also section 2.1.3 for pre-vaccination screening guidelines and section 2.1.4 for general contraindications for all vaccines.

The only specific contraindication to HepB is anaphylaxis following a previous dose, or individuals with a history of allergic reactions to yeast or any of the vaccine's components. This is uncommon. Immunisation of previously infected subjects is wasteful, but not harmful.

See section 14.6 for contraindications and precautions to DTaP-IPV-HepB/Hib vaccine.

8.7 Expected responses and AEFIs

See section 14.7 for expected responses and AEFIs with DTaP-IPV-HepB/Hib vaccine.

8.7.1 Expected responses

Minor side-effects – including local tenderness and redness, nausea, diarrhoea, general malaise and fever – are more common in adults than in children and, except for local reactions, occur at rates close to those seen with a placebo. Minor reactions reported after receiving the vaccine include a temperature >37.7°C in 1–6 percent, pain in 3–29 percent, and erythema, headache or swelling in 3 percent of vaccinees.

8.7.2 AEFIs

Allergic reactions have been reported but are rare. Anaphylaxis is extremely rare.

A number of studies have examined and failed to find disease events linked to hepatitis B immunisation.[38] These studies have documented no increased risk of multiple sclerosis,[39, 40] diabetes, chronic fatigue syndrome,[41] encephalomyelitis or hair loss.[42] Rarely, transient

thrombocytopenia[43] and myalgia and arthralgia[44, 45] have been reported after HepB vaccination.

8.8 Public health measures

The elimination of HBV transmission is now a realistic public health goal,[7, 46] especially with the proven effectiveness and safety record of HepB.[47]

It is important to ensure vaccination programmes are maintained for the at-risk populations, especially babies of mothers with chronic hepatitis B infection.

> It is a legal requirement that all cases of acute hepatitis B infection be notified to the local medical officer of health.

Babies born to HBsAg-positive mothers should be notified at birth. The prevention of perinatal transmission is covered in section 8.5.2.

8.8.1 Passive immunisation

HBIG is prepared from donated blood plasma and contains high levels of anti-HBs antibody (see Appendix 6). It is given after exposure to HBV and provides passive anti-HBs antibody protection against acute and chronic HBV disease. HBIG prophylaxis should be given in combination with the HepB to confer both passive and active immunity after exposure.

The efficacy of HBIG alone in preventing clinical hepatitis B infection is about 75 percent in adults, but the protection lasts only for a few months.[1]

Whenever immediate protection is required, immunisation with a vaccine should be combined with simultaneous administration of HBIG at a different site. It has been shown that passive immunisation with HBIG does not suppress the active immune response to vaccination. A single dose of HBIG (usually 400 IU for adults, 100–110 IU for the newborn; refer to the 'Hepatitis B' chapter of the *Communicable Disease Control Manual 2012*[2]) is sufficient. If infection has already occurred at the time of the first immunisation, virus replication is unlikely to be inhibited completely, but severe illness and, more importantly, the

development of chronic HBV infection may be prevented, particularly in the infants of HBsAg-positive mothers.

The management of contacts is summarised in Table 8.7.

Table 8.7: Management of contacts of hepatitis B cases

Contact	Serological testing of contact (HBsAg, anti-HBs, anti-HBc, IgM and IgG)	Immunoglobulin (if within 7 days of onset of case's symptoms)	Immunisation
Any sexual contact, including protected sex	Yes	Yes, immediately after blood taken	Yes, immediately after blood taken
Household, mucosal or percutaneous	Yes	Yes, if serology negative	Yes, if serology negative
Other	Yes	No	Yes, if serology negative

Source: Ministry of Health. 2012. *Communicable Disease Control Manual 2012*. URL: http://www.health.govt.nz/publication/communicable-disease-control-manual-2012 (accessed 20 March 2017).

For more details on control measures, refer to the 'Hepatitis B' chapter of the *Communicable Disease Control Manual 2012*.[2]

8.9 Variations from the vaccine data sheet

See section 14.9 for variations from the DTaP-IPV-HepB/Hib (Infanrix-hexa) data sheet.

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