

# 3 Hepatitis B

## 3.1 Introduction

Hippocrates described episodes of jaundice, likely to have been viral hepatitis caused by various viruses. In 1883 hepatitis transmitted through blood or blood products was first documented in Germany during a smallpox immunisation campaign. McCallum proposed the term hepatitis B for 'serum' hepatitis in 1947. The Australia antigen, now called the hepatitis B surface antigen (HBsAg), was first identified in 1967 and is the basis of the vaccine.

Hepatitis B virus (HBV) has a high impact on morbidity and mortality throughout the world. In New Zealand, HBV causes more deaths than any other vaccine preventable disease apart from influenza. The long latency period of the virus and the importance of lifestyle factors (in particular, alcohol intake) mean that the impact of HBV is largely invisible. HBV is believed to be second only to tobacco as a cause of human cancers. Superinfection of hepatitis B infected patients with hepatitis D (delta) virus is common in some Pacific peoples and injecting drug users, and can result in exacerbation of liver disease.

When New Zealand introduced universal infant hepatitis B immunisation it was one of the first countries to do so. The World Health Organization (WHO) recommends hepatitis B immunisation, and at least 90 countries have included the vaccine on their immunisation programmes.

In 2005, the countries of the Western Pacific Region of WHO agreed to the target that by 2012 the rate of carriage of HBV in five-year-old children will be reduced to 2 percent. The long-term aim is to reduce carriage of hepatitis B to below 1 percent at the age of five years. New Zealand has had a universal infant immunisation programme for hepatitis B vaccine since 1988 and therefore should have already reached this target. This may be confirmed by the result of the serosurvey being carried out in New Zealand in 2005/06.

## 3.2 The illness

HBV is a partially double stranded DNA virus, composed of a nucleocapsid core (HBcAg) surrounded by an outer lipoprotein coat that contains the surface antigen (HBsAg). A third antigen, HBeAg, is soluble and is released from liver cells with active HBV infection. The presence of HBeAg in the blood indicates a high degree of infectivity (ie, an actively replicating virus). The antigens are identified as indicated above, while their respective antibodies are designated anti-HBc, anti-HBs and anti-HBe.

HBV is usually transmitted by infected blood or exchange of body fluids during sexual intercourse/activity. Although HBV can be found in all body fluids, the blood has most and saliva least. Bond et al<sup>1</sup> have shown that desiccated blood was still

infective after one week (and the antigen remained detectable for several years). Before the immunisation programme in New Zealand, HBV transmission occurred commonly in school aged children. The exact mode of transmission is not clear but could be related to contact with impetigo, or surfaces such as mats or playgrounds that contain crusts from sores. Vertical transmission from mother to infant also occurs, particularly if the mother is HBeAg positive.

The incubation period varies between six weeks and six months (average two to three months). HBsAg may appear within two weeks, but in rare instances may not be apparent until six to nine months. The variation is related to the dose of virus in the inoculum, the mode of transmission and host factors. Blood from experimentally inoculated volunteers has been shown to be infectious many weeks before the onset of the first symptoms, and it remains infective through the acute clinical course of the disease and during the chronic carrier state.

The virus infects liver cells, multiplying there and releasing large amounts of HBsAg, which may be detected in blood during active infection. The virus is not cytopathic itself; rather, the host immune response leads to death of the infected liver cell. There is a spectrum of clinical illness, which includes asymptomatic infection in approximately 60 percent of individuals; sub-acute illness with jaundice, anorexia, nausea and malaise; and fulminant hepatitis, which may be fatal, especially in those over 40 years of age. Acute hepatitis occurs rarely in infants, in approximately 6 percent of infected children and in approximately 33 percent of infected adults. Arthralgias, macular rashes and polyarteritis nodosa may occur early in the course of the illness. Papular acrodermatitis has been noted in children. Because jaundice is not always present with these conditions, the true aetiology of symptoms may not be obvious. Following the acute illness there is a prolonged convalescent phase, often lasting many weeks. Rarely (2 percent) acute hepatitis B may be fatal.

A chronic carrier state (see section 3.3) may develop if infection does not stimulate an effective immune response, and the virus survives in the body and continues to replicate, often for many years. This chronic carrier state is more frequent after infection during infancy and early childhood. The risk of carriage following infection drops from about 90 percent in the first six months of life,<sup>2</sup> to 25–50 percent by five years of age and to 6–10 percent of acutely infected older children and adults. It is unusual for adults to become chronic carriers unless they are immune suppressed. The chronically infected individual often has no history of an acute illness.

Viral antigens remain present for many years in carriers, although 1–6 percent of carriers per year will clear the virus spontaneously. The presence of HBeAg in the blood of a chronic carrier indicates a high degree of infectivity, while the disappearance of HBsAg and the appearance of anti-HBs generally indicate the individual is immune and no longer infectious.

## Screening for carriers

Once detected, carriers can be offered counselling, screening and long term follow-up to detect chronic liver disease and the early stages of hepatocellular carcinoma. Vaccination is offered to susceptible household and sexual contacts of carriers to limit the spread of disease. Treatment with antiviral drugs such as interferon and/or lamivudine are options currently available, although neither is ideal.

Although there remains uncertainty about the population benefit of screening, it is likely that in some individuals the serious outcomes of carriage will be prevented by early detection. In 1999 a screening programme for Māori, Pacific and Asian peoples over 15 years of age was started in the North Island. The programme also enrolled people of other ethnic groups and included follow-up of individuals under the age of 15 years found to carry the HBV. Up to 30 June 2005 there were more than 12,000 clients with chronic hepatitis B actively enrolled on the surveillance programme (with the Hepatitis Foundation as the national provider – see below for contact details) for long term follow-up. If they are identified as carriers, participants are assessed and followed-up by the programme to detect and manage liver disease.

All pregnant women should be screened for hepatitis B carriage antenatally. Administration at birth of hepatitis B immunoglobulin (HBIG) and hepatitis B vaccine prevents mother to infant transmission of hepatitis B virus in 92–95 percent of infants (see section 3.4).

A surveillance and advice service is available from:

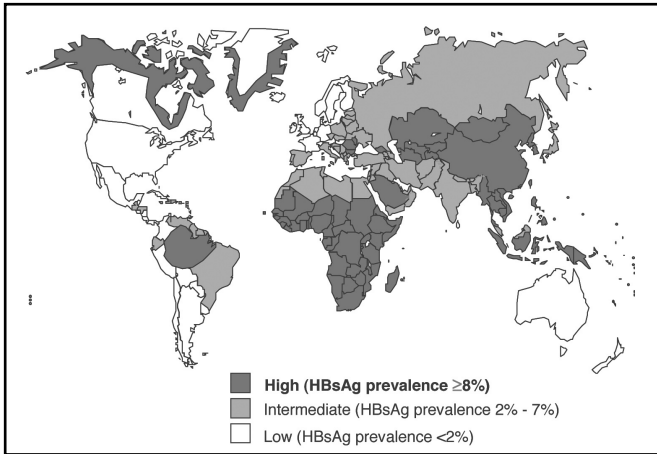
The Hepatitis Foundation  
PO Box 647  
Whakatane  
Phone 07 307 1259 or 0800 332 010.

## 3.3 Epidemiology

Chronic carriers, defined as individuals having HBsAg detectable in their blood for more than six months, are the most common source of hepatitis B infection. The world can be divided into areas of high (8 percent and over), middle (2–7 percent) and low (less than 2 percent) levels of carriage (or endemicity), with 45 percent, 43 percent and 12 percent of the world's population living in those areas, respectively. In areas of high endemicity, the lifetime risk of infection with hepatitis B virus is over 60 percent, and most infections are in the first years of life. The Pacific countries and most of Asia (except Japan and India) are high endemicity countries. In areas of low endemicity, the lifetime risk of infection is less than 20 percent, and most infections are in adult at risk populations (see Figure 3.1).

New Zealand is defined overall as a country with a low endemic level of hepatitis B carriage, but there are areas with medium and high endemic levels (see New Zealand epidemiology below).

**Figure 3.1: WHO geographic pattern of Hepatitis B prevalence, 2001**



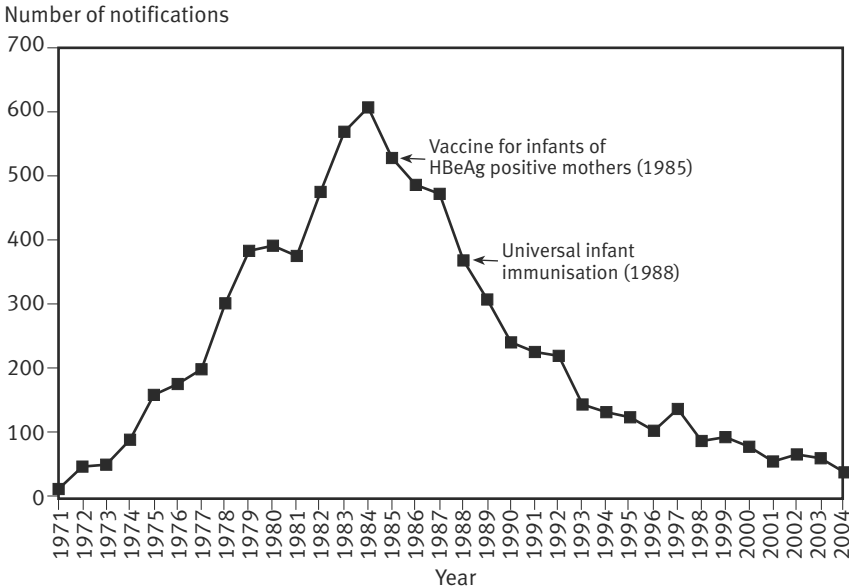
Source: [www.who.int/vaccines-documents/DocsPDF01/www613.pdf](http://www.who.int/vaccines-documents/DocsPDF01/www613.pdf)

The highest risk of transmission is during the perinatal period. If no prophylaxis is given to the infant, the baby of an HBeAg positive carrier 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.

### New Zealand epidemiology

The 1985 National Serum Survey found evidence of past infection in 15 percent of New Zealand children, with generally higher rates in the north and east of the North Island. Milne, Moyes and others showed that in the eastern Bay of Plenty almost half of the population (60 percent of Māori and 30 percent of Europeans) were infected by 15 years of age.<sup>3,4</sup> Prior to vaccination, the lifetime risk of acute icteric hepatitis in this region was 10 percent and the risk of developing the chronic carrier state 9 percent.

**Figure 3.2: Notifications of hepatitis B, 1971–2004**



According to estimates from New Zealand data, chronic carriers have a 5 percent risk of developing chronic active hepatitis or cirrhosis, with perhaps a 2 percent risk of death. The risks are doubled if hepatitis D (delta) virus infection is also present. Hepatocellular carcinoma is estimated to occur in approximately 10 percent of male and 5 percent of female HBsAg carriers. Hepatitis B notifications have declined from about 600 per year in the mid-1980s, when immunisation was introduced, to 61 cases notified in 2003 and 39 cases in 2004 (1.6 per 100,000 population) (see Figure 3.2). The change in the number of notifications of hepatitis B may also be because earlier notifications of hepatitis B included chronic carrier states, whereas only acute cases are under surveillance now. In 2005 there were no cases notified who were less than 15 years of age, and only one case was in the 15–19 years age group.

### History of the New Zealand Immunisation Schedule

Hepatitis B vaccine was added to the Immunisation Schedule gradually, starting in September 1985, when it was offered to newborn babies of HBeAg positive mothers. Three 10 µg doses of plasma derived vaccine were given, as recommended by the manufacturer. In March 1987 the immunisation programme was extended to newborns of mothers with HBsAg and children born in certain high risk districts (Northland, Takapuna, Auckland, South Auckland, Rotorua, Napier and Gisborne).

The demonstration that low dose vaccination was immunogenic enabled the extension of hepatitis B immunisation to everyone born after 29 February 1988. From this date four doses of 2 µg of plasma derived vaccine were given at birth, six

weeks, three months and 15 months of age. There was a catch-up campaign for all preschoolers. The households and sexual contacts of HBsAg positive women identified during antenatal screening were also entitled to free immunisation.

The plasma derived vaccine (H-B-Vax®) was replaced by a genetically engineered recombinant vaccine (ENGERIX-B) from 1 December 1989. This was given at the manufacturer's recommended dose at six weeks, three months and 15 months of age. Babies of carrier mothers also received a dose of vaccine plus HBIG at birth. From February 1990 free hepatitis B immunisation was extended to all children under 16 years of age.

In February 1996 the third dose of hepatitis B vaccine was brought forward from 15 to five months of age to give early protection to infants and to complete the hepatitis B vaccine schedule in the first year of life, when compliance is high. This schedule continues in 2006 with hepatitis B vaccine at age six weeks, three months and five months, plus hepatitis B vaccine and hepatitis B immunoglobulin at birth for a baby whose mother is a carrier of the hepatitis B virus.

### 3.4 Vaccines

All the hepatitis B vaccines currently available are preparations of HBsAg. The vaccines in New Zealand are the yeast and *Escherichia coli* derived vaccines HBvaxPRO® (MSD) and ENGERIX-B (GSK), which have been developed using recombinant DNA technology. Hepatitis B (HBvaxPRO®) vaccine and the combination *Haemophilus influenzae* type b and hepatitis B vaccine (Hib-Hepatitis B, COMVAX®, MSD) are publicly funded for the National Immunisation Schedule.

At the end of 2005, in addition to COMVAX®, the following hepatitis B containing combination vaccines are licensed for distribution in New Zealand:

- HAV-Hep B (hepatitis A and hepatitis B vaccine, TWINRIX and TWINRIX JUNIOR, GSK) (see also section 14.4)
- DTwP-Hib-Hep B (TRITANRIX-HB+Hib, GSK)
- DTaP-Hep B (INFANRIX™-HepB, GSK)
- DTaP-IPV-Hep B (INFANRIX®-penta, GSK)
- DTaP-IPV-Hep B/Hib (INFANRIX®-hexa, GSK).

(Key: D: diphtheria, T: tetanus, wP: whole cell pertussis, aP: acellular pertussis, Hep B: hepatitis B, Hib: *Haemophilus influenzae* type b, IPV: inactivated polio vaccine)

#### Efficacy

Clinical trials in high risk groups have shown a vaccine efficacy of 85 to 95 percent, and virtually complete protection in those who develop antibody levels of  $\geq 10$  mIU/mL (the protective level). At least 95 percent of infants, children and adolescents develop protection after three doses of vaccine.

The response rate drops with age: from 90 percent for adults under 40 years of age, to about 70 percent for those 60 years of age. Smoking, obesity, HIV (human immunodeficiency virus) infection and chronic disease all reduce the response rate, but age is the primary factor affecting response. Some non-responders to the initial vaccination course will produce adequate antibody levels after a further booster dose of vaccine, or a second course. However, persistent non-responders occur, especially those with impaired immune systems or undergoing haemodialysis.

For babies of HBeAg positive mothers, controlled trials have shown that vaccine at birth provides 65–95 percent protection from infection,<sup>5</sup> and correct administration of HBIG with vaccination provides 80–97 percent protection against infection.<sup>6,7,8</sup>

Although the height of the antibody titre determines the length of time the antibody can be detected in the blood, it does not seem important for long term protection. It is probable that once a seroprotective level is reached (a titre of  $\geq 10$  mIU/mL), booster doses of vaccine are unnecessary.<sup>9,10</sup> Children who are given booster doses up to 12 years after the primary series show strong anamnestic responses, and follow-up studies of vaccinees have shown evidence of wild virus infection (anti-HBc) without any clinical illness and without HBsAg. This is despite the fact that a large proportion will lose detectable antibodies (30 to 50 percent after seven years).

Evidence is accumulating that boosters of hepatitis B vaccine are unnecessary provided that the seroprotective level is reached (a titre of  $\geq 10$  mIU/mL). Follow-up of vaccinees in Taiwan who were immunised at birth has shown that protection against hepatitis B infection persisted for at least 15 years, and the programme reduced both perinatal transmission and subsequent horizontal transmission.<sup>11</sup> A follow-up study was undertaken in Alaska<sup>12</sup> on 841 Alaskan natives, 53 percent of a cohort of 1578 individuals, who had been vaccinated with three doses of hepatitis B vaccine starting at age six months or older, including adults. The study found that overall 84 percent had protective levels of antibody after 15 years and the vaccine protected against infection. Both the participants who received hepatitis B vaccine as adults and those who received vaccine in infancy remained protected. Antibody levels decreased most in individuals who received vaccine before the age of four years. Out of the original cohort there were 16 asymptomatic infections which were more frequent in those who had not responded to the original course of vaccine. Only one individual was HBV DNA positive over at least a three year follow-up.

In all populations where it has been measured, immunisation has led to a dramatic drop in HBV carriage. For example, in Alaska carriage dropped from 16 percent to zero 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.<sup>13</sup>

It is important that vaccination against hepatitis B does not encourage relaxation of good infection control procedures. Hepatitis B immunisation does not protect against HIV, hepatitis C or other blood borne viruses.

## Dosage

Follow the manufacturer's recommended dosage for the vaccines in current use (hepatitis B vaccine, HBvaxPRO®, or Hib-Hepatitis B, COMVAX®). It is important that the injection is given intramuscularly, not into dermal fat. In special circumstances hepatitis B vaccine may be given intradermally to increase the immune response (see section 3.5).

The hepatitis B vaccine 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 section 2.3 for needle sites and sizes.)

## 3.5 Recommended immunisation schedule

### Babies of HBsAg positive mothers

Follow the flow chart in Figure 3.3 below.

These children are at high risk of infection (almost certain if the mother is HBeAg positive) and of becoming carriers. At birth, or as soon as possible after (preferably within 12 hours), the first dose of 5 µg of hepatitis B vaccine is given at the same time as HBIG 100 IU, using a separate syringe and different limb. A vitamin K injection may be given at the same time, in the same limb as the HBIG but not at the same site. If administration is inadvertently delayed it should be given as soon as the delay is identified, because such delays are associated with increased risk of infection.

All women should be tested for their HBsAg status during the antenatal period. If a woman's HBsAg status is unknown at the time of delivery, the infant should be given hepatitis B vaccine 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 infant should be given HBIG as soon as possible (preferably within two days).<sup>14</sup> The use of HBIG confers a small additional benefit in preventing carriage, and is recommended given the serious consequences of carriage. The recommended dose of HBIG for neonates is 100 IU.

Subsequent doses are given as per the National Immunisation Schedule: *H. influenzae* type b with hepatitis B vaccine is given at six weeks and three months of age, and the hepatitis B vaccine is given at five months.

At five months of age, as well as giving the hepatitis B vaccine (and the other schedule vaccines), it is essential to take blood to confirm the infant is protected and to identify the 2–3 percent of children who are infected (either from prenatal infection or from failure of prophylaxis), and the similar number of children who are not infected (ie, HBsAg negative) and who have failed to seroconvert. The protective level for adults and children is generally accepted as  $\geq 10$  mIU/mL. However,

for the babies of HBsAg positive mothers who have received HBIG at birth the immunoglobulin may interfere with a test result at five months (see Appendix 8).

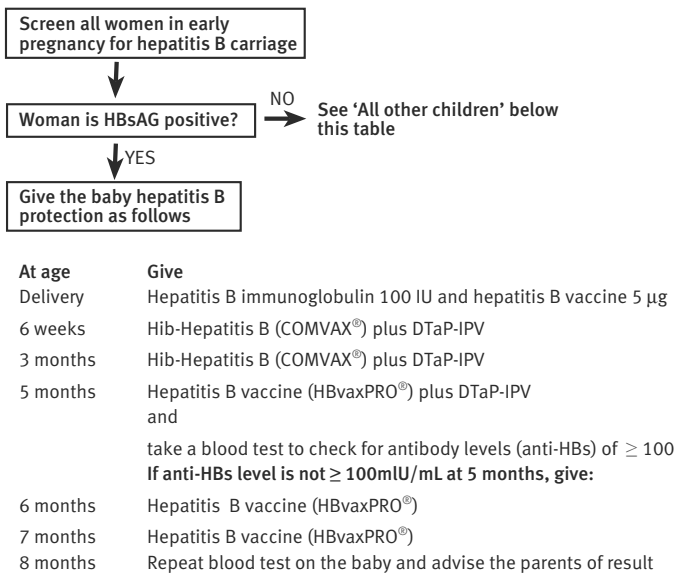
The following recommendations for babies of HBsAg positive mothers at five months of age are:

- Babies with serology of  $\geq 100$  mIU/mL are considered protected.
- Babies with serology of  $< 100$  mIU/mL at five months have an indeterminate result, and a further two doses of vaccine at six and seven months should be given and the serology repeated to test for a protective level of  $\geq 10$  mIU/mL at eight months of age (see also Appendix 8).

If the blood test at five or eight months confirms the carrier state, the parents should be advised accordingly (see Figure 3.3 below).

### Figure 3.3: Recommended screening for hepatitis B of women in early pregnancy and management of a baby of a HBsAg positive woman

All other vaccines are given as on the usual National Immunisation Schedule.



The National Immunisation Register (NIR) will collect data on those infants who receive HBIG and hepatitis B vaccine at birth.

## All other children

The recommended immunisation schedule is for three doses of 5 µg of hepatitis B vaccine at six weeks, three months and five months of age. At six weeks and three months of age the combination vaccine Hib-Hepatitis B is given, and at five months of age the hepatitis B vaccine is used.

## Adolescents and adults

It is recommended (and publicly funded) that adolescents between 11 and 15 years of age who have not previously received a full hepatitis B vaccine course receive two doses of 10 µg hepatitis B vaccine (HBvaxPRO®), with the second dose four to six months after the first.

For adults, the vaccine manufacturers recommend three doses of 10 µg hepatitis B vaccine spaced at zero, one and six months. Shorter intervals between the second and third doses lead to lower antibody levels but adequate protection. In healthy adults a two dose schedule separated by six months,<sup>15</sup> a three dose schedule given over three weeks,<sup>16</sup> and various other accelerated schedules have led to seroconversion rates equivalent to those obtained when following the manufacturer's 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.

## Other recommendations

Hepatitis B immunisation is recommended and publicly funded for the following groups:

- all children up to their 16th birthday – if the hepatitis B vaccine is not given during the first year, three doses of vaccine are recommended (follow the manufacturer's recommendations); a two-dose regime of 10 µg of HBvaxPRO® is recommended for adolescents (from 11 to 15 years of age)
- household and sexual contacts of known carriers – these individuals may be offered hepatitis B immunisation, at monthly intervals at the recommended dosage, unless testing indicates they are already infected or immune
- participants and family members in the hepatitis B screening programme.

Hepatitis B immunisation is also recommended, but not publicly funded, for the following groups (note that employers should fund hepatitis B vaccine for employees at occupational risk):

- adults at risk because of their occupation – including dentists, medical practitioners, nurses, laboratory technologists, physiotherapists, students entering the health professions, orderlies, and other emergency, educational or health care workers who may come into contact with blood or body fluids in the course of their work

- other adults at risk, including:
  - those undergoing renal dialysis, who require a higher dose of vaccine (check manufacturer’s recommendation for this group)
  - adults with chronic liver disease, and prior to liver transplant, who should receive hepatitis B vaccine early in the course of their illness
  - adults with hepatitis C infection, who should receive hepatitis A and B vaccine
  - individuals with haemophilia and other regular recipients of blood products
  - persons (staff and patients) in institutions caring for intellectually disabled individuals
  - prison inmates
  - men who have sex with men
  - injecting drug users
  - people with a high number of sexual partners
  - commercial sex workers.

### **Preterm infants**

In infants of carrier mothers, early protection is vital and these infants must receive HBIG within 12 hours of birth and the vaccine at birth, with subsequent doses of hepatitis B vaccine at the recommended chronological ages (see ‘Babies of HBsAg positive mothers’ section above).

One small study<sup>17</sup> suggests that in very premature infants born to carrier mothers, adequate protection is maintained for up to 59 days by giving HBIG within 12 hours of birth. A decision as to whether to immunise at that stage or give a further dose of HBIG will be made according to the clinical condition of the infant, but the same study indicated that an immune response to hepatitis B vaccine can be mounted by infants with birth weights as low as 1000 grams.

For babies of non-carrier mothers, some studies indicate a reduced response to hepatitis B vaccine in infants less than 37 weeks gestation or less than 2000 grams.<sup>18</sup> In infants of non-carrier mothers, the first dose is normally given at six weeks of age. It is recommended, in the case of neonates born at less than 31 weeks gestation, that the first dose of hepatitis B vaccine be postponed until just before discharge from hospital. (See also section 1.8.)

### **Pregnancy**

Hepatitis B infection in pregnant women may result in severe disease for the mother and active infection of the newborn. 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 partner of an infectious male).

## Testing post immunisation

For the testing schedule for babies of HBsAg positive mothers, see Figure 3.3. Routine testing is not recommended for infants born to non-carrier mothers because almost all will seroconvert.

All those who are likely to be at increased risk of infection should have a blood test one to six months after the last dose of vaccine to ensure they have seroconverted. This includes households and sexual contacts of carriers and those occupationally exposed.

Vaccinees who have anti-HBs levels  $\geq 10$  mIU/mL are protected and will not need boosters. If the level is  $< 10$  mIU/mL one to six months after the last dose is given, an additional dose of vaccine should be given, and another blood sample taken to confirm adequate antibody levels. If negative, complete the course of two further doses and check the blood test at least one month after completion of the course. A study of 76 adults who had not developed protective antibodies after three doses of hepatitis B vaccine found that 75 percent developed specific cellular immune responses that may protect them against viral infection.<sup>19</sup>

For those vaccinated some time ago, and for whom it is unknown whether three doses of hepatitis B vaccine were given, it is recommended that a booster dose be given and serology repeated one month after that dose. If  $\geq 10$  mIU/mL, no further doses should be given; if  $< 10$  mIU/mL, complete the course of three doses of vaccine.

Those who have reached levels of 10 mIU/mL or more do not need any booster doses, even if antibodies subsequently wane to undetectable levels. If exposed, they will have a secondary anamnestic immune response that will prevent replication of the virus.<sup>20,21</sup>

For adults at particular risk of exposure to hepatitis B virus (such as health care workers) who fail to respond to a course of hepatitis B vaccine and do not reach a serology of  $\geq 10$  mIU/mL, a fourth dose of hepatitis B vaccine should be given and serology repeated. This is followed by two further doses at one-month and six-month intervals to complete a second course. Individuals who fail to respond to this second course of vaccine should be considered for a further course of three doses of hepatitis B vaccine given by the intradermal route.

In a small study from Queensland, intradermal hepatitis B vaccine was given to 43 health care workers who had failed to respond to intramuscular hepatitis B vaccine. Thirty-nine individuals (90 percent) developed protective immunity following intradermal vaccination.<sup>22</sup> In another study in Canterbury District Health Board,<sup>23</sup> 27 health care workers who had not responded to previous courses of hepatitis B vaccine were given a further booster dose of hepatitis B vaccine. If they remained non-responders they were given intradermal hepatitis B vaccine at each of four visits, with two intradermal injections given at each visit. Both the GSK and the MSD

vaccine were used in the study; the dose of the MSD (10 µg/mL) vaccine was given as two injections of 1.25 µg, and the dose of the GSK (20 µg/mL) vaccine as two intradermal injections of 2.5 µg. There were local reactions at the injection sites. Following the intradermal course of hepatitis B vaccine, 20 out of the 27 participants had seroconverted, reaching an anti-HBs level of > 10 mIU/mL. The mean level was 126 mIU/mL (with a range of 12–1000 mIU/mL).

### **Pre-vaccination screening**

A discussion on pre-vaccination screening should be part of the informed consent procedure before administering hepatitis B vaccine (see section 2.2). The purpose of pre-vaccination screening is to avoid giving vaccine to those who are carriers or already immune. In particular, vaccination of those who do not know they are carriers may produce a false sense of security about their hepatitis B status. In general, those at higher risk of being a carrier should be encouraged to undergo pre-vaccination screening, while those at low risk may be vaccinated without prior screening. Vaccinating a person who is a carrier does not prevent the future detection of the carrier state, nor cause an increase in adverse reactions.

## **3.6 Expected responses and adverse events following immunisation (AEFI)**

### **Expected responses**

Minor side effects – including local soreness and redness, nausea, diarrhoea, general malaise and fever – are more common in adults than children and, except for local reactions, occur at rates close to those seen with a placebo. Minor reactions reported after the receipt of 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.

### **Adverse events following immunisation**

A number of studies have looked for and failed to find disease events linked to hepatitis B immunisation, including any links with multiple sclerosis,<sup>24,25</sup> diabetes, chronic fatigue syndrome,<sup>26</sup> encephalomyelitis, or hair loss.<sup>27</sup> Rarely, thrombocytopenia<sup>28</sup> and myalgia and arthralgia<sup>29,30</sup> have been reported after hepatitis B vaccine.

Allergic reactions have been reported but appear rare. Anaphylaxis has been reported extremely rarely in adults.

Any severe or unexpected reactions should be reported to CARM, PO Box 913, Dunedin, using the prepaid postcard HP3442 (see section 2.4) or via online reporting at <http://carm.otago.ac.nz>. If the patient or parent/caregiver does not consent to being identified, the report should be made without personal identification.

### 3.7 Contraindications

The general contraindications to all vaccines apply to hepatitis B vaccine (see section 1.9).

The only true specific contraindication to hepatitis B vaccine is anaphylaxis following a previous dose. This is uncommon. Immunisation of previously infected subjects is wasteful, but not harmful, apart from giving a false reassurance to carriers, who remain unaware of their condition and may subsequently assume they are immune.

### 3.8 Control measures

All cases of hepatitis B infection should be notified to the local medical officer of health.

HBIG is available for passive protection and should be used in combination with the hepatitis B vaccine to confer both passive and active immunity after exposure.

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 an active immune response. A single dose of HBIG (usually 400 IU for adults, 100 IU for the newborn) is sufficient for healthy individuals (see Table 3.1). 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 the carrier state may be prevented, particularly in the infants of carrier mothers.

**Table 3.1: Hepatitis B immunoglobulin (HBIG) doses**

Age	HBIG dose
Neonates (under 1 month)	100 IU
1 month to 4 years	200 IU
5 to 9 years	300 IU
10 years to adult	400 IU

Those who should receive HBIG and the hepatitis B vaccine, apart from infants born to carrier mothers (see section 3.5), are:

- non-immune persons who have been accidentally inoculated, or who have contaminated the eye, mouth, fresh cuts or abrasions of the skin with blood from a known HBsAg positive person – individuals who suffer such accidents should wash the contaminated area thoroughly and seek medical advice from the local medical officer of health, the local hospital infection control officer or an occupational health service
- susceptible households and sexual contacts of those with acute hepatitis B, if they are not already carriers or immune. HBIG should be given within seven days of the onset of clinical disease in the index case. Commence vaccination at the

same time. The local medical officer of health can assist with contact tracing and HBIG administration.

Sexual and household contacts of carriers should be immunised but need not receive HBIG.

For more details on control measures, refer to *Control of Communicable Diseases Manual*.<sup>31</sup>

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