

## Hepatitis B

### HEPATITIS B VACCINES FOR AUSTRALIANS: INFORMATION FOR IMMUNISATION PROVIDERS

#### Disease and epidemiology

- Hepatitis B is a viral disease that primarily affects the liver.
- Most infected young children are asymptomatic, but a high proportion become chronically infected, especially if they are infected perinatally.
- A substantial proportion of chronically infected individuals will develop liver cirrhosis and/or hepatocellular carcinoma, which account for considerable morbidity and mortality.
- In Australia, groups with a higher prevalence of chronic hepatitis B infection include persons who inject drugs, Aboriginal and Torres Strait Islander people, migrants from hepatitis B endemic regions, men who have sex with men, and inmates of correctional facilities.
- The hepatitis B virus is transmitted through contact with blood or body fluid of an infectious person, and is commonly acquired either perinatally, by sexual contact, by non-sexual close contact or by exposure to infectious fluids.
- Vaccination is the best way to prevent hepatitis B.

#### Who should be vaccinated

- All infants
- Children/young adolescents – catch-up vaccination for those not previously immunised
- Adults at higher risk of: (1) exposure to hepatitis B infection, due to frequent close contact with infected persons, certain personal risk factors, occupational exposure or travel to areas where hepatitis B is endemic; (2) severe disease, due to certain medical conditions or treatments.

#### Vaccine

- The hepatitis B vaccine is a subunit vaccine containing hepatitis B surface antigen produced by recombinant DNA technology. It is safe and highly effective.
- Different vaccination schedules are recommended for different age groups/settings:
  - For infants: birth dose, then at 2, 4 and 6 months of age
  - For children/adolescents and adults: standard 3-dose schedule (at 0, 1 and 6 months from 1st dose). For adolescents aged 11–15 years: a 2-dose schedule using adult formulation vaccine is also acceptable.
  - Other schedules can be indicated for adults with particular medical conditions and for travellers.

## The disease

Hepatitis B disease is caused by the hepatitis B virus (HBV), a DNA virus. It primarily affects the liver. The virus replicates in the hepatocytes of the liver and may lead to liver dysfunction as well as immune-mediated liver cell damage.<sup>1,2</sup> HBV infection is a major global health problem; it is estimated that >240 million people have chronic hepatitis B<sup>3</sup> and >680,000 deaths occur annually due to complications of hepatitis B infection.<sup>4</sup>

## Clinical features

Infection with HBV can be asymptomatic or manifest as either acute or chronic disease.

The majority of acute HBV infections are not clinically recognised. Acute hepatitis B infection is usually asymptomatic in young children, but symptomatic disease with jaundice occurs in about 30–50% of infected adults.<sup>2,5</sup> Clinical symptoms and signs of viral hepatitis are not specific to hepatitis B, and may include systemic symptoms like fever, malaise, fatigability, anorexia, nausea and vomiting, abdominal pain, and myalgia. In patients who develop jaundice, it usually appears 1–2 weeks after onset of systemic symptoms and lasts about 1–3 weeks. The incubation period from virus exposure to onset of jaundice ranges from about 45 to 180 days, with an average of 90 days.<sup>1,2,6</sup> During convalescence, fatigue and malaise can persist for up to several months. Potentially fatal fulminant hepatitis occurs in approximately 0.5% of acute adult cases, but is rarer in children.<sup>1,2</sup>

A very high proportion (up to 90%) of children infected with HBV in early infancy will become chronically infected.<sup>7</sup> The proportion who become chronically infected decreases with increasing age at infection, to <10% among infected adults.<sup>5,7</sup> Chronic HBV infection is identified by persistence of hepatitis B surface antigen (HBsAg) in the blood for at least 6 months. Clearance of HBsAg among the chronically infected is unusual, occurring in <1% per year.<sup>1</sup> Chronic HBV infection can lead to liver cirrhosis and/or hepatocellular carcinoma (HCC), which are the major contributors to morbidity and mortality of chronic HBV infection.<sup>1,2</sup>

Some chronically HBV infected persons may remain asymptomatic. Symptoms of chronic hepatitis B disease are usually non-specific, unless there is cirrhosis or HCC, and do not correspond to disease severity. It is estimated that 15–25% of people with chronic hepatitis B will die from liver cirrhosis or HCC.<sup>2,8</sup> Prognostic factors include age of HBV

acquisition, HBV viral load, histological type of chronic hepatitis, and aggravating factors like alcohol consumption and co-infection with other hepatotropic viruses.<sup>1,2,8</sup>

## Diagnosis

Specific diagnosis of HBV infection is based on serologic and/or nucleic acid testing.

Hepatitis B surface antigen (HBsAg) and antibodies to the hepatitis B core antigen (anti-HBc antibodies) are markers of infection. The hepatitis B early antigen (HBeAg) is associated with a high level of viral replication and, hence, high infectivity.<sup>1,2,8</sup> Nucleic acid tests are also used in diagnosis and sensitive tests can detect HBV DNA in the serum of an infected person 10–20 days before detection of HBsAg.<sup>2</sup> Antibody against hepatitis B surface antigen (anti-HBs antibody) is a marker of immunity, acquired after either natural infection or vaccination.

## Treatment

Treatment for acute HBV infection is generally supportive.

Current antiviral therapy of chronic hepatitis B does not eradicate HBV. The aim of treatment for chronic HBV infection is to reduce the risk of developing chronic liver disease by sustained suppression of HBV replication in the liver.<sup>9</sup> Long-term treatment with antiviral drugs has been shown to be effective in reducing the risk of both disease progression and of developing HCC. A systematic review found incidence of HCC to be >50% lower among patients on treatment.<sup>10</sup> Patients who are identified as chronically infected with HBV should be referred to a specialist hepatitis clinic for further clinical assessment and consideration of antiviral therapy.

## Epidemiology

HBV is a major global health problem and causes approximately 686,000 deaths worldwide each year.<sup>4</sup> Areas of high endemicity, indicated by HBsAg seroprevalence of 8% or higher, include most of East and South-east Asia (except Japan), Pacific Island groups, parts of central Asia, the Amazon Basin and sub-Saharan Africa.<sup>11</sup> In these regions, infections are mainly acquired perinatally or in early childhood.

## Hepatitis B in Australia

Australia is categorised as a 'low prevalence' country for HBV infection (i.e. <2% of the population is HBsAg-positive). In 2013, HBsAg seroprevalence was estimated at approximately 1.0%. However, this still equates to approximately 210,000 people living with

chronic hepatitis B infection with an estimated 389 deaths due to chronic HBV infection in Australia in 2013.<sup>12</sup> Population groups with higher prevalence of chronic hepatitis B, compared with the general Australian population, include:<sup>13,14</sup>

- persons who inject drugs
- Aboriginal and Torres Strait Islander people
- migrants from hepatitis B endemic regions
- men who have sex with men
- inmates of correctional facilities.

In Australia, various hepatitis B vaccination programs that targeted individuals at increased risk of infection were implemented beginning in the late 1980s. Australia introduced universal vaccination for all infants in 2000. Adolescent hepatitis B catch-up vaccination programs were implemented at different times, in different settings, in different jurisdictions, from 1997.<sup>15</sup>

Laboratory-confirmed hepatitis B cases are notifiable in all jurisdictions of Australia. The overall notification rate of ‘newly acquired hepatitis B’ (i.e. where laboratory results indicate that infection was acquired within the previous 24 months) decreased from 1.2 per 100,000 in 2009 to 0.7 per 100,000 in 2013.<sup>12</sup> Notification rates of newly acquired hepatitis B were consistently low across this period in children aged <15 years and declined substantially among people aged 15–29 years.<sup>12</sup> Adolescent catch-up immunisation programs may have contributed to this decrease in young adults.

## HBV transmission

Humans are the only natural reservoir for HBV. Transmission of HBV may result from inoculation through broken or penetrated skin, or by mucosal contact with blood or other body fluids (mainly vaginal fluids and semen) from an infectious person. HBV is about 50 to 100 times more infectious than the human immunodeficiency virus (HIV).

The major modes of transmission of HBV are:

- from mother to child, around the time of birth (perinatal)
- sexual contact
- non-sexual contact with an infected person, including household transmission (e.g. child-to-child through contact between open sores or wounds)

- through other skin-penetrating or mucous membrane exposures to blood or other bodily fluids; common scenarios include:
  - sharing of needles and other injecting drug equipment
  - inadequately sterilised skin penetrating instruments (e.g. tattooing equipment, body-piercing equipment, acupuncture needles)
  - needle-stick injury (e.g. in a healthcare setting)
  - contact between infective body fluids and mucous membranes.

HBV can survive outside the body for up to 7 days and hence can also be transmitted via contaminated inanimate objects.<sup>16</sup>

The practice of screening donated blood has virtually eliminated the risk of transmission of HBV through blood transfusion in Australia.<sup>17</sup>

In Australia, hepatitis B infection is most commonly acquired in early adult life by horizontal transmission (e.g. through injecting drug use and unprotected sex).<sup>18</sup> Injecting drug use was the most frequently reported source of exposure (where a source was identified) among notifications of newly acquired hepatitis B in 2009–2013.<sup>12</sup>

To prevent transmission of HBV to others, persons who are HBsAg-positive should use barrier protection during sexual intercourse if their partners are non-immune, avoid sharing toothbrushes or razors with others, cover any open cuts and scratches, and not donate blood, organs or sperm. Any blood spills from these persons should be cleaned with detergent or bleach.<sup>9</sup> Vaccination should be recommended for their household contacts, and vaccination plus hepatitis B immunoglobulin for sexual contacts (see [Sexual exposure](#)).

Persons, including children, who are HBsAg-positive do not need to be excluded from participating in day care or school or other activities, including contact sports; they can share food or utensils with others, or kiss others.<sup>9</sup>

## Who should be vaccinated<sup>19</sup>

### A) All infants, as part of the National Immunisation Program (NIP)

#### B) Children and young adolescents

Australian children born since May 2000 would have been eligible for infant hepatitis B vaccination under the NIP.

Adolescents about 11–15 years of age (school years 6–8) who had not been previously vaccinated with the hepatitis B vaccine were offered a catch-up course through school-based vaccination programs in all Australian states and territories up until 2013.

Unvaccinated children and adolescents can receive the vaccine through vaccination providers such as GPs.

#### C) Adults with increased risk of exposure to HBV or severe hepatitis B disease

Non-immune (anti-HBc and anti-HBs antibody negative) adults with increased risk of exposure to HBV, or risk of a more serious outcome if infected with HBV, are recommended to be vaccinated (see [Box A](#)).

## Vaccine

### Formulations and schedules

The hepatitis B-containing vaccines registered in Australia are subunit vaccines that contain HBsAg, produced by recombinant DNA technology from yeast cells. These vaccines are available either as monovalent antigen formulations or in combination with other vaccine antigens.

Monovalent hepatitis B vaccine comes in paediatric (0.5 mL), adult (1 mL) and adult dialysis (1 mL) formulations. The formulations of the different brands are different, and the quantity of HBsAg in their corresponding age-appropriate formulations also differs. For any of the brands, the specific age-appropriate formulation is to be used.

Although switching of brands is generally not recommended, in scenarios where the brand of vaccine used for previous doses is not known, any age-appropriate formulation may be used, as there is no reason to suggest that use of a different brand of the currently available formulations in Australia (Engerix-B and H-B-Vax II) will compromise immunogenicity or safety.<sup>20-22</sup>

Those who are also at risk of hepatitis A exposure should consider receiving the age-appropriate

formulation of a combination hepatitis A/hepatitis B vaccine (see [Table 1](#)).

There are specific formulations and schedules for different age groups and for individuals with certain conditions (see below and also [Table 1](#)).

#### A) Infants

A single **birth dose** of hepatitis B vaccine, using the monovalent paediatric formulation, is recommended for all newborn infants in Australia. The birth dose should be given as soon as the baby is medically stable, and preferably within 24 hours of birth, but may be administered within the first 7 days after birth. This birth dose aims to prevent transmission of HBV to the infant in the first months of life from the mother or household or other close contact who may have HBV infection. (All newborns of mothers with chronic HBV infection should be given hepatitis B immunoglobulin as well as a birth dose of hepatitis B vaccine, preferably on the day of birth.)

Studies have shown that the birth dose of the vaccine is well tolerated by newborn infants. There is no evidence that the birth dose interferes with either the establishment or maintenance of breastfeeding and it is not associated with an increased risk of either fever or medical investigations for sepsis in the newborn.<sup>23-25</sup>

Following the birth dose of monovalent hepatitis B vaccine, **3 doses of a hepatitis B-containing vaccine** (the combination vaccine also used for protection against diphtheria, tetanus, pertussis, polio and *Haemophilus influenzae* type b, 'DTPa-hepB-IPV-Hib') are recommended for all infants, to be given at 2, 4 and 6 months of age. Thus a total of 4 doses of hepatitis B vaccine are recommended in the first year of life. This is consistent with the NIP schedule. However, infants who miss the birth dose of monovalent hepatitis B vaccine do not require a catch-up dose, and should receive the 3 doses of a hepatitis B-containing combination vaccine at 2, 4 and 6 months of age as per the NIP schedule (see [Table 1](#)).<sup>19</sup> If any of the doses recommended as part of the infant primary schedule have been missed, advice on planning catch-up can be found in *The Australian Immunisation Handbook* (Chapter 2.1).<sup>19</sup>

#### B) Children and adolescents aged <20 years

The standard 3-dose schedule with a paediatric vaccine formulation can be used. This consists of 3 doses of the monovalent vaccine, with the 2nd and 3rd doses given 1 and 6 months, respectively, after the 1st dose (a '0, 1, 6 months' schedule) (see [Table 1](#)).

For **adolescents aged 11–15 years**, a 2-dose schedule using an **adult** vaccine formulation, with the 2nd dose given 4–6 months after the 1st dose, is an alternative to the 3-dose schedule (see [Table 1](#)). This 2-dose schedule produces similar levels of protective antibodies,<sup>26,27</sup> while compliance to the vaccination schedule may be improved.<sup>28</sup>

#### **C) Adults with increased risk of exposure to HBV**

The standard 3-dose schedule with an adult vaccine formulation can be used (see [Table 1](#)). There is some flexibility regarding the intervals between the vaccine doses in the 3-dose schedule. This may be required in some specific settings where a balance between, on the one hand, maximising compliance with the recommended schedule and thus the likely antibody response and, on the other hand, maximising the vaccination uptake in the shortest possible time in a high-risk but hard-to-reach population has to be achieved. If a shortened 3-dose schedule needs to be used, all three of the following minimum interval requirements must be satisfied in order to attain comparable antibody levels to the standard 3-dose schedule:<sup>19</sup>

- minimum interval between the 1st and 2nd doses of 1 month,
- minimum interval between the 2nd and 3rd doses of 2 months, and
- minimum interval between the 1st and 3rd doses of 4 months (or 16 weeks).

#### **D) Adults with particular medical conditions**

Dialysis patients, HIV-positive adults and other immunocompromised adults require larger than usual doses of hepatitis B vaccine.

##### *Adult haemodialysis patients*

There are two alternatives:

- (a) 1.0 mL of Engerix-B adult formulation (20 µg) in each arm on each occasion (i.e. effectively giving a double dose on each occasion) in a 0, 1, 2, 6 months 4-dose schedule;<sup>29</sup> or
- (b) a single dose of H-B-Vax II dialysis formulation (40 µg) on each occasion in a 0, 1 and 6 months 3-dose schedule.

##### *HIV-positive adults*

Limited studies in HIV1-positive adults have demonstrated a stronger and accelerated serological response to a schedule that consists of 4 double doses using Engerix-B, comprising two injections of the

standard adult dose on each occasion, in a 0, 1, 2, 6 months schedule.<sup>30,31</sup>

#### **E) People travelling to hepatitis B endemic areas who have an imminent risk of exposure**

Engerix-B (paediatric or adult formulations) and Twinrix (720/20) are also registered for use in 4-dose accelerated vaccination schedules (see [Table 2](#)). An accelerated schedule is only recommended for persons with an imminent risk of exposure when there is limited time for completion of the vaccination course before departure to a hepatitis B endemic area. Anti-HBs antibody levels are substantially lower after 3 accelerated doses than after the standard 3-dose schedule; hence, a 4th dose should be administered to these people at 12 months to provide long-term protection.

#### **Administration**

Hepatitis B vaccines are administered by intramuscular injection. The two common injection sites are the anterolateral aspect of the thigh (for infants and children aged <12 months) and the deltoid muscle (for older children and adults).

#### **Immune response to vaccination**

Protective efficacy of hepatitis B vaccination is mediated not only by anti-HBs antibodies but also the induction of immune memory. An anti-HBs antibody concentration of  $\geq 10$  mIU/mL, measured about 1–2 months after completion of a primary vaccine course, is a reliable marker of clinical protection. The standard 3-dose schedule induces protective levels of neutralising antibody against HBV in more than 90–95% of vaccine recipients aged <40 years.<sup>2,6,8</sup> Known factors for poorer response include ageing (>40 years), smoking, obesity, HIV infection, and some chronic or immunocompromising diseases.<sup>2,6</sup> The frequency of seroconversion increases progressively from about 35% after the 1st dose to more than 90% after the 3rd dose.

## **Box A: Adults with increased risk of exposure to HBV or severe hepatitis B disease for whom vaccination is recommended**

For more details, refer to the latest update of *The Australian Immunisation Handbook* available on the Immunise Australia website ([www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home](http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home)).

### **A) Individuals who may have frequent close contact with infected persons**

- Aboriginal and Torres Strait Islander people
- Migrants from hepatitis B endemic regions
- Household contacts of persons (of any age) with acute or chronic hepatitis B infection
- Persons who attend either residential or non-residential day-care facilities for persons with developmental disabilities\*
- Sexual contacts of persons with hepatitis B<sup>†</sup>

### **B) Individuals who have some personal risk factors**

- Men who have sex with men\*
- Persons who inject drugs\*
- Inmates of long-term correctional facilities\*

### **C) Individuals with medical conditions placing them at higher risk of exposure to HBV and/or more serious outcome if infected with HBV**

- Adult haemodialysis patients and persons with severely impaired renal function
- HIV-positive adults and other immunocompromised adults
- Persons with clotting disorders who receive blood product concentrates and persons with recurrent transfusion requirements
- Persons with chronic liver disease and/or hepatitis C\*
- Solid organ and haematopoietic stem cell transplant recipients\*<sup>‡</sup>

### **D) Individuals with occupational risks**

- Healthcare workers who are directly involved in patient care
- Workers who have regular contact with human tissue, blood or body fluids and/or used needles or syringes, including embalmers, funeral workers, tattooists and body-piercers
- Sex industry workers
- Staff or volunteers working in care facilities for persons with developmental disabilities\*
- Members of the police or the armed forces, emergency services workers and staff of correctional facilities, if they are assigned to duties that may involve potential exposure to human tissue, blood or body fluids

*Note:*

- (i) Staff of child day-care centres will normally be at minimal risk of exposure to HBV – specific advice may be sought from your local public health authority if necessary.
- (ii) Contact sports generally carry a low risk of hepatitis B transmission. However, age-appropriate hepatitis B vaccination is recommended.

### **E) Travellers to areas of intermediate or high hepatitis B endemicity\***

\* The combined hepatitis A/hepatitis B vaccine should be considered for non-immune persons in the groups marked with an asterisk (\*), due to the concurrent risk of exposure to and/or benefit of protection against hepatitis A.

† Non-immune susceptible sexual partners of persons who are HBsAg-positive should be offered post-exposure hepatitis B immunoglobulin and hepatitis B vaccination; both should be initiated within 14 days of the last sexual contact.

‡ Solid organ transplant recipients should be vaccinated before the transplantation as they may be at increased risk of infection from the transplanted organ. Haematopoietic stem cell transplant recipients should be revaccinated following transplantation due to the loss of immune memory that often follows the transplant.

**Table 1: Recommended schedules for use of monovalent hepatitis B and hepatitis B combination vaccines<sup>19</sup>**

Vaccine	Age of vaccine recipient	Dose (HBsAg protein)	Volume per dose (mL)	Number of doses	Recommended schedule intervals*†
<b>Recommended infant schedule</b>					
Enerix-B (paediatric formulation) or H-B-Vax II (paediatric formulation)	birth	10 µg (Enerix-B) or 5 µg (H-B-Vax II)	0.5	1	Birth (if not given at birth, may be given up to 7 days of age)
Combination hepatitis B-containing vaccine (e.g. Infanrix hexa DTPa-hepB-IPV-Hib)	2, 4 and 6 <sup>‡</sup> months	10 µg	0.5	3	1st dose: 2 months of age <sup>§</sup> 2nd dose: 4 months of age (2 months after 1st dose) 3rd dose <sup>‡</sup> : 6 months of age (2 months after 2nd dose)
<b>Monovalent hepatitis B vaccines – standard 3-dose schedule</b>					
Enerix-B (paediatric formulation)	<20 years	10 µg	0.5	3	1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 6 months after 1st dose
Enerix-B (adult formulation)	≥20 years	20 µg	1.0	3	1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 6 months after 1st dose
H-B-Vax II (paediatric formulation)	<20 years	5 µg	0.5	3	1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 6 months after 1st dose
H-B-Vax II (adult formulation)	≥20 years	10 µg	1.0	3	1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 6 months after 1st dose
H-B-Vax II (dialysis formulation)	≥20 years	40 µg	1.0	3	1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 6 months after 1st dose
<b>Monovalent hepatitis B vaccines – 2-dose schedule ONLY for adolescents aged 11–15 years</b>					
Enerix-B (adult formulation)	11–15 years	20 µg	1.0	2	1st dose: day 0 (day of vaccination) 2nd dose: 6 months after 1st dose
H-B-Vax II (adult formulation)	11–15 years	10 µg	1.0	2	1st dose: day 0 (day of vaccination) 2nd dose: between 4 and 6 months after 1st dose
<b>Combination hepatitis A/hepatitis B vaccines</b>					
Twinrix (720/20) <sup>¶</sup>	1–<16 years	20 µg	1.0	2	1st dose: day 0 (day of vaccination) 2nd dose: between 6 and 12 months after 1st dose (2-dose schedule)
Twinrix Junior (360/10)	1–<16 years	10 µg	0.5	3	1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 6 months after 1st dose
Twinrix (720/20)	≥16 years	20 µg	1.0	3	1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 6 months after 1st dose

\* For minimum intervals, refer to text above. For more detailed advice on minimum intervals, in particular in catch-up situations, refer to *The Australian Immunisation Handbook*.<sup>19</sup>

† In these schedules, the 'day 0' dose refers to the day when the 1st dose is given (i.e. day 0 of the vaccination course), not the age of the recipient. For infant vaccination, where the 1st dose is a 'birth dose' it is indicated as so.

‡ The final dose of the primary course for infants should preferably be given at ≥24 weeks of age. For more detailed advice on upper age thresholds, in particular in catch-up situations, refer to *The Australian Immunisation Handbook*.<sup>19</sup>

§ The 2 month dose can be given as early as 6 weeks of age.

¶ This schedule should not be used for those who require prompt protection against hepatitis B, for example, if there is close contact with a person known to be chronically infected with hepatitis B.

**Table 2: Accelerated hepatitis B vaccination schedules (for persons with imminent risk of exposure)<sup>19</sup>**

Vaccine	Age of vaccine recipient (years)	Dose (HBsAg protein)	Volume (mL)	Number of doses	Recommended schedule minimum interval
Engerix-B (paediatric formulation)	<20	10 µg	0.5	4	1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 2 months after 1st dose 4th dose: 12 months after 1st dose
Engerix-B (adult formulation)	≥20	20 µg	1.0	4	1st dose: day 0 (day of vaccination) 2nd dose: 1 month after 1st dose 3rd dose: 2 months after 1st dose 4th dose: 12 months after 1st dose or 1st dose: day 0 (day of vaccination) 2nd dose: 7 days after 1st dose 3rd dose: 21 days after 1st dose 4th dose: 12 months after 1st dose
Twinrix (720/20)	≥16	20 µg	1.0	4	1st dose: day 0 (day of vaccination) 2nd dose: 7 days after 1st dose 3rd dose: 21 days after 1st dose 4th dose: 12 months after 1st dose

### Booster doses

Booster doses of hepatitis B vaccine after completion of a primary course by a recommended schedule are not recommended for immunocompetent persons, as there is good evidence that a completed primary course of hepatitis B vaccination provides long-lasting protection, even though vaccine-induced antibody levels may decline with time and may become undetectable.<sup>2,6,19,32,33</sup> This applies to children and adults, including healthcare workers.

However, booster doses are recommended for some individuals:

- Persons who are immunocompromised, particularly those with HIV infection or renal failure. The time for boosting in such persons should be decided by regular monitoring of anti-HBs levels at 6- to 12-monthly intervals.<sup>34</sup>
- Preterm infants born at <32 weeks gestation or whose birth weight was <2000 g. A booster dose of a hepatitis B-containing vaccine is recommended at 12 months of age, unless an anti-HBs level measured at ≥1 month after the final dose of the primary course is ≥10 mIU/mL.

### Vaccine safety and adverse events

Hepatitis B vaccines are safe.<sup>2,8,35,36</sup> Frequently reported adverse events following immunisation include pain/soreness at the site of injection (3–29% of vaccine recipients), fever >37.7°C (1–6%), headache, injection site swelling and redness (about 3% for each).<sup>37</sup> The estimated incidence of anaphylaxis among children administered hepatitis B vaccine is very rare (about 1 in 1.1 million doses).<sup>38</sup> Other rare adverse events such as

Guillain-Barré syndrome and arthritis have been reported following hepatitis B vaccination; however, there is no evidence of a causal relationship with hepatitis B vaccination. Multiple studies and review panels have concluded that there is no link between multiple sclerosis and hepatitis B vaccination.<sup>6,37,39,40</sup>

### Who should be tested for hepatitis B serology before vaccination<sup>19</sup>

Routine antenatal screening of all pregnant women for HBsAg is recommended to allow for appropriate measures to prevent HBV infection in infants.

Serological testing for evidence of past (or current) hepatitis B infection prior to hepatitis B vaccination may be warranted, particularly in those with increased risk of acquiring hepatitis B infection (see [Box A](#)), to facilitate timely appropriate clinical management and prevention of transmission.

### Who should be tested for hepatitis B surface antibodies (anti-HBs) after vaccination

Routine post-vaccination serological testing is not recommended, except in the following circumstances.

Infants born to mothers who are chronically infected with HBV should be tested for serologic markers of HBV infection, 3–12 months following completion of their full primary course of hepatitis B vaccination.

Post-vaccination serological testing is recommended 4–8 weeks after completion of the primary course for persons in the following categories:<sup>19</sup>

- those at substantial occupational risk (e.g. healthcare workers whose work involves frequent exposure to human tissue, blood or body fluids)



- those at risk of severe or complicated HBV disease (e.g. persons who are immunocompromised, and persons with pre-existing liver disease not related to hepatitis B)
- those in whom a poor response to hepatitis B vaccination may occur (e.g. haemodialysis patients, persons with bleeding disorders vaccinated via the subcutaneous route)
- sexual partners and household, or other close household-like, contacts of persons who are infected with hepatitis B.

If adequate anti-HBs levels ( $\geq 10$  mIU/mL) are not reached on serological testing 4–8 weeks after the final vaccine dose, the possibility of HBV infection should be investigated and, if excluded, the person should be managed as a non-responder – see [below](#)).

Persons who are at substantial occupational risk who have a documented history of a primary course of hepatitis B vaccine, without historical evidence of seroconversion (i.e. those not tested after completion of the primary course) but with a current anti-HBs level  $< 10$  mIU/mL, should be given a single booster dose (the 4th dose) of vaccine, with testing for anti-HBs antibody 4 weeks later. If the anti-HBs level remains  $< 10$  mIU/mL, the possibility of HBV infection should be investigated. If the anti-HBs level is  $\geq 10$  mIU/mL, the person is regarded as immune.

#### **Persons who do not respond to the primary vaccination course**

A ‘non-responder’ is a person who has a documented history of a primary course of hepatitis B vaccine, but with an anti-HBs level  $< 10$  mIU/mL (measured 4–8 weeks after the primary course). Approximately 5–10% of adult vaccine recipients do not respond to the primary series (3 doses) of hepatitis B vaccine.<sup>41</sup>

Non-responders who have had chronic HBV infection excluded should be offered further doses of the vaccine. There are a number of potential options, including administering a 4th double dose; administering a further course of 3 doses at monthly intervals; or intradermal administration of doses. Further serological testing should be conducted, at least 4 weeks after the last dose. Refer to *The Australian Immunisation Handbook* for more details.<sup>19</sup>

Persistent non-responders should be informed of their status and advised on how to minimise exposure to HBV, and specifically on the need to receive hepatitis B immunoglobulin within 72 hours of percutaneous or permucosal exposure to HBV.

#### **Pregnancy and breastfeeding**

Hepatitis B vaccination is not routinely recommended for pregnant or breastfeeding women. However, the WHO advises that neither pregnancy nor breastfeeding is a contraindication to the use of hepatitis B vaccines.<sup>6</sup>

#### **Contraindications**

Persons who have had hypersensitivity reactions to yeast or any hepatitis B vaccine components should not receive the vaccine. Persons who experienced serious adverse events following a previous dose of hepatitis B vaccine should seek specialist advice before receiving further doses of the vaccine.

#### **Other considerations**

##### **Use of hepatitis B vaccine after potential exposure to hepatitis B**

##### **Infants born to mothers who are chronically infected with hepatitis B**

The birth dose of hepatitis B vaccine should be given to these infants, preferably within 24 hours of birth. A dose of hepatitis B immunoglobulin (HBIG; 100 IU) is also necessary, preferably within 12 hours of birth and certainly within 48 hours of birth. Testing of antibody response 3–12 months after completion of the full vaccination course is recommended for these infants. Refer to *The Australian Immunisation Handbook* for more details.<sup>19</sup>

##### **Sexual exposure**

Non-immune susceptible sexual partners of HBsAg-positive persons should be offered post-exposure HBIG and hepatitis B vaccination; both should be initiated within 14 days of the last sexual contact. Refer to *The Australian Immunisation Handbook* for more details.<sup>19</sup>

##### **Persons exposed to blood, body fluids or blood-contaminated secretions**

Following significant exposure (percutaneous, ocular or mucous membrane) to blood or body fluids that may potentially contain HBV, where feasible, the source individual should be tested for HBsAg as soon as possible. Depending on the source individual’s HBsAg status and the exposed person’s immune status, vaccination and HBIG may be required. Refer to *The Australian Immunisation Handbook* for more details.<sup>19</sup>

## Additional resources for primary medical care/vaccination providers

- *The Australian Immunisation Handbook*, 10th edition – the most up-to-date clinical recommendations are contained in the online version of the *Handbook* [www.immunise.health.gov.au/internet/immunise/public/shing.nsf/Content/Handbook10-home](http://www.immunise.health.gov.au/internet/immunise/public/shing.nsf/Content/Handbook10-home)
- Immunise Australia website [www.immunise.health.gov.au](http://www.immunise.health.gov.au)
- National Immunisation Program schedule [www.immunise.health.gov.au/internet/immunise/public/shing.nsf/Content/national-immunisation-program-schedule](http://www.immunise.health.gov.au/internet/immunise/public/shing.nsf/Content/national-immunisation-program-schedule)
- Australasian Society for HIV Medicine. *B positive – all you wanted to know about hepatitis B: a guide for primary care providers*. 2nd edition (2014) [www.ashm.org.au/resources/Pages/1976963310.aspx](http://www.ashm.org.au/resources/Pages/1976963310.aspx)
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