

Primary prevention of hepatitis B virus infection

KEY POINTS

- Universal vaccination programs for hepatitis B have had a profound impact on reducing the incidence of hepatitis B virus (HBV) infection.
- All infants should receive hepatitis B vaccination, with the first dose given at birth in the first 24 hours.
- Infants born to mothers positive for hepatitis B surface antigen (HBsAg) should receive both hepatitis B immunoglobulin and the first dose of hepatitis B vaccine, administered concomitantly, within 12 hours of birth.
- For HBsAg-positive women with high viral loads (> 200,000 IU/mL), consider use of antiviral therapy to further reduce the risk of mother-to-child transmission.
- It is recommended that adolescents not vaccinated in childhood receive hepatitis B vaccines.
- Individuals at risk of exposure should be vaccinated.
- The Australian Immunisation handbook (update 2017) contains current recommendations and is an important resource for clinicians <http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home>

Introduction

Primary prevention of hepatitis B virus (HBV) infection includes:

- vaccination of non-immune individuals at risk of infection
- prevention of mother-to-child transmission, including routine antenatal testing of all women, universal infant immunisation, and appropriate management and follow-up of both hepatitis B surface antigen (HBsAg)-positive women during pregnancy and their infants (see: [Managing hepatitis B virus infection in pregnancy and children](#))
- universal precautions to prevent exposure and post-exposure prophylaxis for individuals exposed to potentially infectious body fluids (see: [Infection control and occupational health](#)).

Aims of vaccination

Hepatitis B vaccination aims to prevent HBV infection and its complications, which include fulminant hepatitis, cirrhosis, liver failure and hepatocellular carcinoma (HCC). In acute cases, fulminant hepatitis occurs rarely, but it is associated with significant mortality, especially in infants (2).

The World Health Organization (WHO) strategy for the control of HBV infection aims to provide universal infant hepatitis B immunisation, with the first dose given at birth (3). By the end of 2015, global coverage for hepatitis B vaccine in routine childhood vaccination schedules reached 185 countries (84%) (4). The vaccine induces antibodies to hepatitis B surface antigen (anti-HBs), and a titre of 10 mIU/mL or more is considered to be protective against HBV infection. With the introduction of universal infant vaccination programs in countries with a high prevalence of hepatitis B (e.g. Taiwan), universal hepatitis B vaccination programs have had a profound impact on reducing the incidence of chronic infection, dropping the HBsAg prevalence rate in children from 10% to 1% (5), and halving the incidence of HCC in children aged 6–14 years (6-8).

Target groups for vaccination in Australia

Target groups for adult vaccination in Australia are essentially the same groups in whom testing for evidence of chronic infection should be considered (see: [Hepatitis B virus testing and interpreting test results](#)) (9). High-priority groups include:

- household, close and sexual contacts of people with chronic hepatitis B (CHB)
- Aboriginal and Torres Strait Islander peoples
- people from countries that have a high- or intermediate-prevalence of hepatitis B.

Other priority groups that should be offered testing and vaccination include men who have sex with men, people living with hepatitis C or human immunodeficiency virus (HIV), people who inject drugs, people in custodial settings and people in at-risk professions. A complete list of the groups that should be considered for vaccination is given in [Table 5.1](#).

Table 5.1 Groups at risk of exposure or significant morbidity from exposure to HBV infection that should be targeted for vaccination

The Australian National Immunisation program	<ol style="list-style-type: none">1. Infants – recommended as part of routine childhood immunisation and funded for children under the Immunise Australia Program. The first dose is given at birth, followed by another three doses at 2, 4 and 6 months of age2. Adolescents – recommended for adolescents who have not yet received a primary course of hepatitis B vaccine
People at higher risk of hepatitis B virus infection	<ol style="list-style-type: none">1. Household, family and other close contacts of people with acute or chronic hepatitis B2. Sexual contacts of people with hepatitis B3. Migrants from hepatitis B-endemic countries4. Men who have sex with men5. Sex workers6. Aboriginal and Torres Strait Islander peoples

	<ol style="list-style-type: none"> 7. People who inject drugs 8. Inmates or staff of correctional facilities 9. People adopting a child from a country with high-prevalence rates 10. Travellers to hepatitis B-endemic areas, either long-term or frequent travellers, and those likely to undertake exposure-prone activities 11. Vulnerable populations including the homeless and people with mental health issues
People prone to exposure or at risk of significant morbidity from exposure	<ol style="list-style-type: none"> 1. Haemodialysis patients 2. People with clotting disorders and others who may need multiple blood or blood-product transfusions, especially if given overseas 3. HIV-positive and other immunosuppressed people 4. Transplant recipients 5. People with chronic liver disease or hepatitis C 6. Clients and staff of facilities for the intellectually disabled
People at risk of occupational exposure	<ol style="list-style-type: none"> 1. Health-care workers 2. People who have had accidental exposure (e.g. tattooists, body piercers, dentists) 3. Contact sports generally carry a low risk of hepatitis B infection. However, age-appropriate hepatitis B vaccination is recommended 4. Child-care workers 5. Embalmers 6. People working in accident and emergency services (e.g. paramedics, police, state emergency service, volunteer first aid givers – Red Cross, St John Ambulance)
<p>As there are state and territory differences, primary-care providers should check with their local health departments for information on which of these groups may be entitled to funded vaccination. <<add link to resource page>></p>	
<p>See The Australian Immunisation Handbook for further information (1) http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home</p>	

Transmission of HBV through blood transfusion and organ transplant has been almost entirely eliminated through the screening of blood and organ donors in Australia. However, there remains a small risk of exposure to HBV for patients with clotting disorders who receive blood-product concentrates.

The modes of transmission still relevant in Australia include:

- vertical or mother-to-child transmission
- household contact
- sexual contact
- re-use of injecting or tattooing equipment
- occupational exposure.

In addition to screening blood donors, organ donors and health-care workers for HBV, the strategy to control HBV infection in Australia includes universal hepatitis B vaccination of neonates and the administration of hepatitis B immunoglobulin (HBIG) at birth to neonates born to HBsAg-positive mothers. In the Northern Territory, the hepatitis B vaccine has been routinely administered to Aboriginal and Torres Strait Islander newborns since 1988, and to all newborns since August 1990. The universal infant program began in 2000, with the first dose given at birth. Hepatitis B vaccination for all adolescents commenced in 1997 in some Australian states and territories, but has now been phased out because those immunised for hepatitis B in the infant program have reached adolescence. Non-immune adolescents and adults younger than 20 years should still be considered for vaccination through the current National immunisation Program expansion, a funded catch up program. For further information see <https://beta.health.gov.au/health-topics/immunisation>

Recommendations for vaccination

The national recommendations for vaccinations are given in the latest edition of the Australian Immunisation Handbook (1). [Table 5.2](#) summarises the vaccines available in Australia.

Table 5.2 Vaccines available in Australia	
Monovalent vaccines	
Trade name (formulation)	Dose of HBsAg protein and volume
Engerix-B (adult formulation ≥ 20 years old)	20 µg in 1 mL
Engerix-B (paediatric formulation < 20 years old)	10 µg in 0.5 mL
H-B-VAX II (adult formulation ≥ 20 years old)	10 µg in 1 mL
H-B-VAX II (paediatric formulation < 20 years old)	5 µg in 0.5 mL
H-B-VAX II (dialysis formulation)	40 µg in 1 mL
Combinations containing hepatitis A vaccine	
Twinrix Junior (1 ≤ 16 years old) (360/10)	10 µg in 0.5 mL
Twinrix (≥ 16 years old)(720/20)	20 in 1 mL
Combination vaccines used in infant vaccination or catch-up schedules	
Trade name (formulation)	Type of combination

Infanrix Hep B (paediatric)	diphtheria-tetanus-acellular pertussis-hepatitis B
Infanrix Hexa (paediatric)	diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliomyelitis vaccine- <i>Haemophilus influenzae</i> type b
Infanrix Penta (paediatric)	diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliomyelitis vaccine

Infants

It is recommended that all newborns receive hepatitis B vaccine within 24 hours of birth, followed by three further doses in infancy, at 2, 4 and 6 months of age. The first dose can be given at 6 weeks of age. If an infant did not receive the birth dose within 7 days of birth, no catch up of that dose is necessary; these infants only require a three-dose course of a hepatitis B-containing combination vaccine, given at 2, 4 and 6 months of age. There should be an interval of at least 8 weeks between doses two and three. For infants the final dose of the primary hepatitis B vaccine course should be administered at or after 24 weeks of age. The type of hepatitis B vaccine used differs between states and territories (1).

Premature infants

Preterm babies do not respond as well as term babies to hepatitis B vaccine (11). For babies under 32 weeks gestation or less than 2000 g birth weight, it is recommended to give the vaccine at 0 (within 24 hours of birth), and 2, 4 and 6 months of age and do one of the following:

- measure anti-HBs at 7 months of age and, if antibody titre is less than 10 mIU/mL, give a booster at 12 months of age (1)
- give a booster at 12 months of age without measuring the antibody titre (19).

Infants born to mothers positive for hepatitis B surface antigen with chronic hepatitis B

Infants born to HBsAg-positive mothers should be given HBIG (100 IU) in addition to the birth dose of monovalent hepatitis B vaccine (19) (see: [Managing hepatitis B virus infection in pregnancy and children](#)). Ideally HBIG should be given within 12 hours and certainly within 48 hours of birth (1). The birth dose of HBV vaccine should be given at the same time but in separate sites. Monovalent vaccine alone has been shown to be protective and should not be delayed; it is most effective given within 24 hours of birth. In all infants, HBsAg and anti-HBs should be measured at 9–12 months of age (i.e. 3–12 months after completing the course of primary vaccination). If the anti-HBs level is less than 10 mIU/mL, further testing for evidence of HBV infection is advised.

Adolescents

It is recommended that adolescents not vaccinated in childhood receive hepatitis B vaccines (1). Two regimens are available:

- Three-dose regimen for adolescents aged up to 20 years: hepatitis B (paediatric formulation) – three doses of 0.5 mL. The optimal interval is 1 month between the first and second dose, and a third dose 5 months after the second dose.
- Two-dose regimen for adolescents aged 11–15 years: H-B-Vax II 10 µg (adult formulation) or Engerix-B 20 µg (adult formulation) at 0 and 4–6 months.

State and territory health authorities can provide further information on hepatitis B vaccine for this age group.

Adults aged 20 years or over

Groups recommended for vaccination (after testing) are listed in [Table 5.1](#).

Monovalent hepatitis B vaccine is usually given in a three-dose schedule, at 0, 1 and 6 month or 0, 2 and 4 month intervals (1). The minimum interval is 1 month between the first and second doses, 2 months between the second and third doses, and 4 months between the first and third doses. Special consideration is needed for immunocompromised individuals, who may require alternative dosing regimens including double dosing.

The standard three-dose schedule is effective in achieving protective antibody titres in over 90% of immunocompetent adults with seroconversion rates of approximately 35% after the first dose and rising thereafter.

Accelerated vaccination schedules

Two products, Engerix-B (paediatric and adult) and Twinrix (720/20), are registered for use in accelerated schedules, which consist of four doses in total. Accelerated schedules should only be used if there is limited time before departure to endemic regions, or the need to achieve urgent protection (9). Whilst accelerated schedules result in a higher proportion of individuals with protective anti-HBs titres in the early months, antibody levels are lower than the standard schedule at 7 months. Thus, the fourth booster dose should always be given in this setting. ([Table 5.3](#)).

Table 5.3 Accelerated hepatitis B vaccination schedules				
Vaccine	Age	Dose (HBsAg protein)	Volume	Schedule
Engerix-B (paediatric)	Up to 20 years	10 µg	0.5 mL	0, 1, 2 months; booster at 12 months
Engerix-B (adult)*	≥ 20 years	20 µg	1.0 mL	0, 7, 21 days; booster at 12 months or 0, 1, 2 months; booster at 12 months (preferred schedule)
Twinrix (720/20)*	> 15 years	20 µg	1.0 mL	0, 7, 21 days; booster at 12 months

*If time permits, it is recommended that the 0, 1, 2 month schedule be used, because higher seroprotective rates are observed following this schedule than with a 0, 7, 21 day schedule; a booster dose at 12 months is recommended for long-term protection.

Booster doses

Although vaccine-induced antibody levels decline with time and may eventually become undetectable, booster doses are not recommended in immunocompetent people after a primary course, because there is good evidence that a completed primary course of hepatitis B vaccination provides long-lasting protection. This recommendation includes health-care workers. Booster doses are recommended, however, for people who are immunocompromised (e.g. those with HIV infection or renal failure) (1). The time for receipt of the boosting dose in these individuals should be determined by monitoring of anti-HBs levels.

Hepatitis B testing before vaccination

Testing before vaccination is recommended for those at increased risk of infection (see: [Hepatitis B virus testing and interpreting test results](#), and [Table 5.4](#)), including people born overseas in high- or intermediate-prevalence countries, Aboriginal and Torres Strait Islander peoples, men who have sex with men, people who inject drugs, sex workers, immunocompromised people and people in custodial settings, or those who have ever been in such settings.

Table 5.4 Prevalence of chronic hepatitis B in Australia by risk group (10)

Group	HBsAg prevalence in risk group (%)	Proportion of CHB in Australia (%)
People born in high- or intermediate-prevalence countries	2.4 (average) 3.6 (Asia-Pacific region) 2.7 (Africa/Middle East) 1.0 (Europe)	56
Aboriginal and Torres Strait Islander peoples	3.7	9
People who inject drugs	4	6
Men who have sex with men	3	4
Non-indigenous Australian-born individuals*	0.3	19
Other or not stated	1.0	6

*excluding those belonging to the other priority populations listed above

CHB: chronic hepatitis B; HBsAg: hepatitis B surface antigen

Hepatitis B testing post vaccination

Infants born to HBsAg-positive mothers should be tested 3–12 months after the primary course of vaccination is completed. Testing for post-vaccination response 4 weeks after the primary course is also recommended for:

- health-care workers involved with exposure-prone procedures (see: [Infection control and occupational health](#))
- those at risk of severe or complicated disease (e.g. immunosuppressed patients and patients with chronic liver disease)
- those expected to have a poor response to hepatitis B vaccine (e.g. haemodialysis patients)
- those at high risk of acquiring hepatitis B (e.g. contacts of those with CHB, people who inject drugs, sex workers, and those living in communities with high prevalence of hepatitis B).

Adverse events following hepatitis B vaccination

Adverse events that can occur following hepatitis B vaccination include:

- soreness at the injection site (5%), fever (usually low grade, 2–3%), nausea, dizziness, malaise, myalgias and arthralgias. Fever can be expected in some neonates (0.6–3.7%) ([1](#)).
- anaphylaxis has been reported in adults, but only rarely ([1](#)).
- although various adverse events (e.g. demyelinating diseases, multiple sclerosis, Guillain-Barré syndrome and arthritis) have been reported, there is no evidence of a causal relationship with these events and hepatitis B vaccination ([1](#), [12](#), [13](#)).

Hepatitis B immunoglobulin

HBIG is prepared from pooled plasma from the blood bank, with samples selected on the basis of high levels of anti-HBs. Its use is recommended in infants born to HBsAg-positive mothers and to non-immune people exposed to hepatitis B virus.

HBIG should be given to the newborns of HBsAg positive mothers within 12 hours of birth, or to adults not previously vaccinated, or non-immune, within 72 hours of exposure, because efficacy diminishes with time from 48 hours after exposure.

The hepatitis B vaccine can be given at the same time as HBIG or within 7 days of exposure. Previous vaccination in the exposed adult should be verified by evidence of detectable anti-HBs. If the anti-HBs is undetectable, HBIG dose should be as follows:

- 100 IU children (< 30 kg weight)
- 400 IU (> 30 kg weight).

Non-response or vaccination failure

A non-responder is a person who has a documented history of an age-appropriate primary course of hepatitis B vaccine, but has never achieved an anti-HBs level of over 10 mIU/mL. In such cases, being positive for HBsAg should first be excluded as a cause of failure in vaccine non-responders. For those subjects who have not achieved adequate anti-HBs levels (≥ 10 mIU/mL) after the third dose of vaccine, a

single booster dose (fourth dose) can be given, and anti-HBs checked 4 weeks later. If the anti-HBs level is over 10 mIU/mL the person can be regarded as immune. People who are non-responders after the fourth booster dose should be given two further doses at monthly intervals, followed by testing for response 4 weeks after the second dose. A few small studies have reported success with administration of high-dose formulations of double-dose administration for the fourth or subsequent doses. Persistent non-responders should be informed about the need for HBIG within 72 hours of parenteral exposure to HBV. A few small studies have indicated that some people respond to intradermal routes of Engerix –B vaccine administration(14).

Vaccination failure may occur in people exposed to HBV variants with mutations in the HBV surface gene (vaccine-induced escape mutant). Most such vaccine-induced escape mutants were initially reported in neonates through vertical transmission and in transplant recipients. These vaccine-induced escape mutants were responsible for most of the 3.4% vaccine failure rate reported in the Chinese adult population undergoing a hepatitis B vaccination program (15).

Hepatitis B vaccination during pregnancy and breastfeeding

Hepatitis B vaccination during pregnancy is not routinely recommended. The vaccine can be given to susceptible pregnant women for whom it would otherwise be recommended, including for post-exposure prophylaxis in non-immune women exposed to a HBsAg-positive source (1). Vaccination is not contraindicated in breastfeeding, and breastfeeding in the vaccinated infant by an HBsAg-positive mother poses no additional risk of viral transmission, despite evidence of HBV in breast milk (16).

For further information about these recommendations, please refer to the latest edition of The Australian Immunisation Handbook (19).

Information on access to free vaccination in each state and territory

Vaccination is provided free for priority populations by a number of State and Territory Governments and can be ordered by GPs through the health department. See State or Territory below for details and information on accessing vaccine. Vaccination for household and sexual contacts of those with HBV is provided free in the ACT, NSW, NT, QLD, SA, VIC and WA.

Australian Capital Territory

Contact the Immunisation Branch to order vaccine.

New South Wales

Groups eligible for free vaccination

GP order form for free vaccine

Northern Territory

Vaccination for some groups is funded by the Northern Territory Department of Health - contact your local Centre for Disease Control

Queensland

Groups eligible for free vaccination

Order form for free vaccine

South Australia

Groups eligible for free vaccination

Order form for free vaccine

Victoria

Groups eligible for free vaccination

Order form for free vaccine

Tasmania

Contact the Public Health Hotline

Western Australia

Information regarding <http://www.health.wa.gov.au/circularsnew/attachments/250.pdf> (see appendix 3)

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