3.6 HEPATITIS B

Virology

Hepatitis B virus (HBV) contains partially double-stranded DNA. The outer surface of the virus is glycolipid which contains the hepatitis B surface antigen (HBsAg). Other important antigenic components are hepatitis B core antigen (HBcAg), and hepatitis B e antigen (HBeAg). HBcAg is not detectable in serum, but can be detected in liver tissue in people with acute or chronic hepatitis B infection. Antibodies developed to HBsAg (anti-HBs) indicate immunity, whereas persistence of HBsAg denotes infectivity, which is greater if HBeAg and HBV DNA are positive.[1]

Clinical features

In approximately 30 to 50% of adults, infection causes symptomatic acute hepatitis, but in young children, particularly those <1 year of age, infection is usually asymptomatic. The incubation period is 45 to 180 days and the period of communicability extends from several weeks before the onset of acute illness usually to the end of the period of acute illness. Acute illness is indistinguishable from other forms of hepatitis, and symptoms include fever, jaundice, malaise, anorexia, nausea and vomiting, abdominal pain (especially in the right upper quadrant), myalgia, and the passage of dark-coloured urine and light-coloured stools. Jaundice may be preceded by an acute febrile illness with arthralgia or arthritis and rash, most typical of hepatitis B. During recovery, malaise and fatigue may persist for many weeks. Fulminant hepatitis occurs in approximately 1% of acute cases.[1,2]

Following acute infection, 1 to 10% of those infected as adults[2,3] and up to 90% of those infected as neonates[1,2] remain persistently infected for many years (see Figure 3.6.1). Chronically infected carriers of HBV are identified by the long-term presence (longer than 6 months) of circulating HBsAg.[4]

Figure 3.6.1: The influence of age of infection with the hepatitis B virus on the likelihood of becoming a hepatitis B carrier

(Modified and used with permission from: Edmunds WJ, Medley GF, Nokes DJ, Hall AJ, Whittle HC. The influence of age on the development of the hepatitis B carrier state. *Proceedings. The Royal Society Biological Sciences.*1993;253:197-201.)

Carriers of HBV are capable of transmitting the disease, though often remain asymptomatic and may not be aware that they are infected. Most of the serious complications associated with hepatitis B infection occur in HBV carriers. Chronic active hepatitis develops in more than 25% of carriers, and up to 25% die prematurely of cirrhosis or hepatocellular carcinoma.[1,2]

Epidemiology

The prevalence of HBV carriage differs in different parts of the world, and may be quite variable within countries. Carrier rates vary from 0.1 to 0.2% among Caucasians in the United States, northern Europe and Australia, 1 to 5% in the Mediterranean countries, parts of eastern Europe, China, Africa, Central and South America, and some Australian Aboriginal populations, and greater than 10% in many sub-Saharan African, southeast Asian and Pacific island populations.[5-7] First-generation immigrants usually retain the carrier rate of their country of origin, but subsequent generations show a declining carrier rate irrespective of vaccination.[5]

Transmission of hepatitis B may result from percutaneous inoculation or mucosal contact with blood or sexual secretions from an HBsAg-positive individual. Screening of blood and organ donors has virtually eliminated the risk of transmission of hepatitis B through blood transfusion and organ transplants.[8,9] Saliva may also contain levels of virus which are likely to be infective only if inoculated directly into tissue (ocular or mucous membranes). Transmission by inadvertent parenteral inoculation, such as by toothbrush, razor etc., through close personal contact in households in which 1 or more carriers or other infected individuals reside, is a low but significant risk.

Routes of transmission include:

- sharing injecting equipment (such as occurs in injecting drug use),
- needle-stick injury, and other types of parenteral inoculation,

- sexual contact (including heterosexual or homosexual intercourse, although the latter has a higher risk),
- transmission from infected mother to neonate (vertical transmission), usually occurring at or around the time of birth,
- child-to-child (horizontal) transmission, usually through contact between open sores or wounds,
- breastfeeding,[10]
- nosocomial transmission in overseas healthcare facilities if infection control procedures are unsatisfactory.

Australian vaccination policy

The initial strategy for the control of hepatitis B in Australia commenced in 1988, targeting groups at particular risk of infection for vaccination at birth. In addition to vaccine, hepatitis B immunoglobulin (HBIG) was given if the mother was a hepatitis B carrier. In 1990, universal infant vaccination commenced in the Northern Territory. In 1996, the NHMRC recommended a universal hepatitis B vaccination program for infants and adolescents. The adolescent program commenced in some States and Territories in 1997 and the universal infant program, with the first dose given at birth, began nationally in 2000. The adolescent program will continue until those immunised for hepatitis B in the childhood program reach adolescence.

Vaccines

- **Engerix-B –** GlaxoSmithKline (recombinant DNA hepatitis B vaccine). **Adult formulation** – Each 1.0 mL monodose vial contains 20 µg recombinant hepatitis B surface antigen (HBsAg) protein, adsorbed onto 0.5 mg aluminium hydroxide. **Paediatric formulation** – Each 0.5 mL monodose vial contains 10 µg HBsAg protein, adsorbed onto 0.25 mg aluminium hydroxide. Both formulations contain traces of yeast proteins and thiomersal (<2 µg/mL). Both are available in packs of 10.
- **H-B-VAX II** – CSL Biotherapies/Merck & Co Inc (recombinant DNA hepatitis B vaccine). **Adult formulation preservative free** – Each 1.0 mL pre-filled syringe or vial contains 10 µg recombinant HBsAg protein, adsorbed onto 0.5 mg aluminium hydroxide. May contain yeast proteins. **Paediatric formulation preservative free –** Each 0.5 mL pre-filled syringe or vial contains 5 µg recombinant HBsAg protein, adsorbed onto 0.25 mg aluminium hydroxide. May contain yeast proteins. Both are available in packs of 10. **Dialysis formulation preservative free –** Each 1.0 mL vial contains 40 µg recombinant HBsAg protein, adsorbed onto 0.5 mg aluminium hydroxide. May contain yeast proteins. Available as single pack only.

Combination vaccines that include both DTPa and hepatitis B

- **Infanrix hexa** – GlaxoSmithKline (DTPa-hepB-IPV-Hib; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliomyelitis vaccine-*Haemophilus influenzae* type b (Hib)). The vaccine consists of *both* a 0.5 mL pre-filled syringe containing 30 IU diphtheria toxoid, 40 IU tetanus toxoid, 25 µg pertussis toxoid (PT), 25 µg filamentous haemagglutinin (FHA), 8 µg pertactin (PRN), 10 µg recombinant HBsAg, 40 D-antigen units inactivated polioviruses type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett) adsorbed onto aluminium hydroxide/phosphate; phenoxyethanol as preservative; traces of formaldehyde, polymyxin and neomycin *and* a vial containing a lyophilised pellet of 10 µg purified Hib capsular polysaccharide (PRP) conjugated to 20–40 µg tetanus toxoid. The vaccine *must be reconstituted* by adding the entire contents of the syringe to the vial and shaking until the pellet is completely dissolved. May also contain yeast proteins.
- **Infanrix Penta** – GlaxoSmithKline (DTPa-hepB-IPV; diphtheria-tetanus-acellular pertussis-hepatitis B-inactivated poliomyelitis vaccine). Each 0.5 mL pre-filled syringe contains 30 IU diphtheria toxoid, 40 IU tetanus toxoid, 25 µg PT, 25 µg FHA, 8 µg PRN, 10 µg recombinant HBsAg, 40 D-antigen units inactivated polioviruses type 1 (Mahoney), 8 D-antigen units type 2 (MEF-1) and 32 D-antigen units type 3 (Saukett) adsorbed onto aluminium hydroxide/phosphate; phenoxyethanol as preservative; traces of formaldehyde, polymyxin and neomycin. May also contain yeast proteins.

Other combination vaccines that include hepatitis B

- **COMVAX** – CSL Biotherapies/Merck & Co Inc (Hib (PRP-OMP)-hepatitis B). Each 0.5 mL monodose vial contains 7.5 µg PRP conjugated to 125 µg meningococcal protein, 5 µg hepatitis B surface antigen; 225 µg aluminium hydroxide; 35 µg borax. May contain yeast proteins.
- **Twinrix Junior (360/10)** – GlaxoSmithKline (formaldehyde inactivated hepatitis A virus (HM175 strain) and recombinant hepatitis B vaccine). Each 0.5 mL monodose vial or pre-filled syringe contains 360 ELISA units of HAV antigens, 10 µg recombinant DNA hepatitis B surface antigen protein; 0.225 mg aluminium phosphate/hydroxide; 0.5% w/v phenoxyethanol; traces of formaldehyde and neomycin. May contain yeast proteins.
- **Twinrix (720/20)** – GlaxoSmithKline (formaldehyde inactivated hepatitis A virus (HM175 strain) and recombinant hepatitis B vaccine). Each 1.0 mL monodose vial or syringe contains 720 ELISA units of HAV antigens, 20 µg recombinant DNA hepatitis B surface antigen protein; 0.45 mg aluminium phosphate/hydroxide; 0.5% w/v phenoxyethanol; traces of formaldehyde and neomycin. May contain yeast proteins.

Hepatitis B vaccines are prepared using recombinant technology. After purification, the HBsAg protein is adsorbed onto elemental aluminium (as hydroxide and/or phosphate). Preservatives, including thiomersal, may be added. Hepatitis B vaccines may contain up to 1% yeast proteins (but no yeast DNA).

Thiomersal-free vaccines, such as H-B-VAX II preservative free paediatric formulation, are now available and are recommended for administration to newborns and infants.[11] Engerix-B paediatric formulation contains a trace amount of thiomersal (<2 µg/mL). All other infant and childhood hepatitis B-containing combination vaccines, such as Infanrix Penta, Infanrix hexa, COMVAX and Twinrix Junior (360/10), are thiomersal-free.

Transport, storage and handling

Transport according to *National Vaccine Storage Guidelines: Strive for 5*.[12] Store at +2°C to +8°C. Do not freeze.

Dosage and administration

Monovalent hepatitis B vaccines are white, slightly opalescent liquids. Any visible change in the product, such as an amorphous flocculent or a granular precipitate may indicate incorrect storage conditions.

(i) Administer by deep IM injection.

(ii) 3-dose regimen

For children and young adults <20 years of age, a total of 3 doses of 0.5 mL of paediatric formulation is recommended. The optimal interval is 1 month between the first and second doses and a third dose 5 months after the second dose. The use of longer time intervals between doses does not impair the immunogenicity of hepatitis B vaccine, especially in adolescents and young children.[13,14] The *minimum interval* between the second and third doses is 2 months.

(iii) For adults ≥20 years of age, a full course of hepatitis B vaccine consists of 3 doses of 1 mL of adult formulation. There should be an interval of 1 to 2 months between the first and second doses with a third dose 2 to 5 months after the second dose (this schedule applies to both Engerix-B and H-B-VAX II). The *minimum interval* between the second and third doses is 2 months.

This induces protective levels of neutralising antibody against hepatitis B virus in more than 90% of adults. The frequency of seroconversion increases progressively from approximately 35% after the first injection to more than 90% after the third injection. There is evidence of immunity (anti-HBs) in most vaccinated subjects after administration of 2 doses of the 3-dose vaccine regimen. However, the third dose is necessary to increase the percentage of responders and to provide long-term protection.

(iv) Alternative 2-dose regimens

A randomised controlled trial, involving 1026 adolescents, demonstrated that adolescents 11–15 years of age who received 2 doses of the adult formulation at 0 and 4–6 months, developed similar protective antibody levels to those vaccinated using the paediatric formulations in the standard 3-dose regimen administered at 0, 1 and 6–12 months.[15]

An open label comparative study in adults found increased compliance among those receiving a 2-dose schedule (86%) over those who completed the 3-dose schedule (18%). Antibody responses were found to be similar among the 2 groups.[16]

A 2-dose schedule used in the 11–15 years age group will improve compliance and provide comparable immunogenicity to that of a 3-dose paediatric schedule. Adolescents (11–15 years of age) can be vaccinated with H-B-VAX II 10 µg (adult formulation) or Engerix-B 20 µg (adult formulation) in a 2-dose regimen of 0 and 4–6 months (H-B-VAX II) or 0 and 6 months (Engerix-B). In older adolescents up to the age of 19 years, in whom compliance with a 3-dose paediatric dosing schedule is in doubt, a 2-dose schedule using an adult formulation may also be used in order to improve protection.

When protection is required against both hepatitis A and hepatitis B in children 1–15 years of age, administration of Twinrix (720/20) in a 2-dose regimen at 0 and 6–12 months results in protective antibody levels for both hepatitis A and hepatitis B (see Table 3.6.1).

Table 3.6.1: Hepatitis B and hepatitis A/hepatitis B combination vaccination schedules

Vaccine	Age	Dose (HBsAg protein)	Volume	Schedule (mo=months)
Monovalent hepatitis B vaccines				
Engerix-B (paediatric)	<20 years	10 µg	0.5 mL	0, 1, 6 mo (3-dose schedule)
Engerix-B (adult)	11–15 years	20 µg	1.0 mL	0, 6 mo (2-dose schedule)
Engerix-B (adult)	≥20 years	20 µg	1.0 mL	0, 1, 6 mo (3-dose schedule)
H-B-VAX II (paediatric)	<20 years	5 µg	0.5 mL	0, 1, 6 mo (3-dose schedule)
H-B-VAX II (adult)	11–15 years	10 µg	1.0 mL	0, 4–6 mo (2-dose schedule)
H-B-VAX II (adult)	≥20 years	10 µg	1.0 mL	0, 1, 6 mo (3-dose schedule)
H-B-VAX II (dialysis formulation)	≥20 years	40 µg	1.0 mL	0, 1, 6 mo (3-dose schedule)
Combination hepatitis A/B vaccines				
Twinrix (720/20)*	1– <16 years	20 µg	1.0 mL	0, 6–12 mo (2-dose schedule)
Twinrix Junior (360/10)	1– <16 years	10 µg	0.5 mL	0, 1, 6 mo (3-dose schedule)
Twinrix (720/20)	≥16 years	20 µg	1.0 mL	0, 1, 6 mo (3-dose schedule)

* This schedule should not be used for those who require prompt protection against hepatitis B; for example, if there is close contact with a known hepatitis B carrier.

(v) Accelerated schedule

Engerix-B formulations (paediatric and adult) and Twinrix (720/20) are registered for use in accelerated schedules. Accelerated schedules should only be used if there is very limited time before departure to endemic regions (see Table 3.6.2).

Table 3.6.2: Accelerated hepatitis B vaccination schedules*

Vaccine	Age	Dose (HBsAg protein)	Volume	Schedule (mo=months)
Engerix-B (paediatric)	<20 years	10 µg	0.5 mL	0, 1, 2, 12 mo
Engerix-B (adult)	≥20 years	20 µg	1.0 mL	0, 1, 2, 12 mo or 0, 7, 21 days, 12 mo
Twinrix (720/20)	≥16 years	20 µg	1.0 mL	0, 7, 21 days, 12 mo

* As higher seroprotective rates are seen after the 0, 1, 2 month schedule, it is recommended that the 0, 7, 21 days schedule be used only in adults and only in exceptional circumstances. In both schedules, a booster dose at 12 months is recommended for long-term protection.

Recommendations

(i) Infants and young children

A birth dose of thiomersal-free monovalent hepatitis B vaccine, followed by doses given in combination vaccines (such as DTPa-hepB, DTPa-hepB-IPV, DTPa-hepB-IPV-Hib or Hib (PRP-OMP)-hepB) at 2, 4 and either 6 or 12 months, is recommended for all children.

The rationale for the universal birth dose is not only to prevent vertical transmission from a carrier mother (recognising that there may be errors or delays in maternal testing, reporting, communication or appropriate response), but also to prevent horizontal transmission in the first months of life from a carrier among household or other close contacts.[17] The birth dose should be given as soon as the baby is physiologically stable, and preferably within 24 hours of birth. Every effort should be made to administer the vaccine before discharge from the obstetric hospital.

Extensive experience indicates that the birth dose of hepatitis B vaccine is very well tolerated by newborn infants. It does not interfere with either the establishment or maintenance of breastfeeding, and it is not associated with an increased risk of either fever or medical investigation for sepsis in the newborn.[18-20]

If an infant has missed the birth dose and is aged 8 days or older, a catch-up schedule is not required. A primary course of a hepatitis B-containing

combination vaccine should be given at 2, 4 and either 6 or 12 months of age (provided the mother is HBsAg negative).

NB. All babies (preterm or term) of carrier mothers must be given a birth dose of hepatitis B vaccine *and* HBIG.

Management of infants born to hepatitis B carrier mothers

Routine antenatal screening for HBsAg is essential for correct implementation of the strategy to prevent newborn infants from becoming infected with, and therefore carriers of, HBV. It also has benefits of enabling appropriate follow-up and management of a carrier, identification of the immune status of other household members, and protection of those who are susceptible to HBV infection. Infants born to HBsAg positive mothers should be given HBIG and a dose of thiomersal-free monovalent hepatitis B vaccine on the day of birth. The dose of HBIG is 100 IU to be given by IM injection. Administration of HBIG is preferable within 12 hours of birth, as its efficacy decreases markedly if administration is delayed beyond 48 hours after birth.

The first dose of monovalent hepatitis B vaccine should be given at the same time as HBIG, but in the opposite anterolateral thigh, as soon as possible – preferably within 24 hours of birth, and definitely within 7 days. This regimen results in seroconversion rates of more than 90% in neonates, despite concurrent administration of HBIG. If concurrent administration is not possible, vaccination should not be delayed beyond 7 days after birth as (providing it is given early) vaccine alone has been shown to be effective in preventing carriage.[21] Three subsequent doses of a multivalent/combination vaccine should be given at 2, 4 and either 6 or 12 months of age (depending on the vaccine used), so that the infant is given a total of 4 doses of hepatitis B-containing vaccines.

Preterm babies

Preterm babies do not respond as well to hepatitis B-containing vaccines as term babies.[22-25] Thus, for babies at <32 weeks' gestation or <2000 g birth weight, it is recommended to give vaccine at 0, 2, 4 and 6 months of age and either:

(a) measure anti-HBs at 7 months of age and give a booster at 12 months of age if antibody titre is <10 mIU/mL, or

(b) give a booster at 12 months of age without measuring the antibody titre.

(ii) Adolescents

Vaccination of adolescents 10 to 13 years of age is recommended for all those in this age group who have not already received a primary course of hepatitis B vaccine. Please refer to your State/Territory health authority for further information (see Appendix 1, *Contact details for Australian, State and Territory Government health authorities and communicable disease control*).

(iii) Adults for whom hepatitis B vaccination is recommended

Note: the combined hepatitis A/hepatitis B vaccine should be considered for susceptible individuals in the groups marked with an asterisk ***(*)****.*

- **Household contacts of acute and chronic hepatitis B carriers**

There is a low, but definite, risk of transmission from a person with acute or chronic hepatitis B. This can be reduced by avoiding contact with blood or other body fluids and not sharing household items which can penetrate skin (such as combs, nail brushes, toothbrushes and razors).

The risk of contacts acquiring hepatitis B infection varies according to the HBeAg status of the carrier, and with cultural and socioeconomic factors. However, it should be recognised that in many situations, family members may have been exposed by the time the risk is recognised. Testing before planned vaccination is recommended for such families, as well as for members of families who have migrated from high prevalence countries.

- **Sexual contacts**

Susceptible (anti-HBc and anti-HBs negative) sexual partners of patients with acute hepatitis B should be offered post-exposure HBIG and hepatitis B vaccination; both should be initiated within 14 days of the last sexual contact. Susceptible partners of asymptomatic carriers should also be offered vaccination.

Hepatitis B is relatively common in clients of sexual health services and vaccination should be offered to susceptible individuals at the time of first attendance.

*Sexually active men who have sex with men should be vaccinated, unless they are already HBsAg positive or have serological evidence of immunity. The combined hepatitis A/hepatitis B vaccine may be appropriate for men who have sex with men, if they are not immune to either disease, as they are at increased risk of both.

- **Haemodialysis patients, HIV-positive individuals and other adults with impaired immunity**

Dialysis patients, HIV-positive individuals and other adults with impaired immunity should be given a larger than usual dose of hepatitis B vaccine. Adults should be given either (i) 1 mL of normal adult formulation in each arm on each occasion (double dose), or (ii) a single dose of dialysis formulation vaccine on each occasion, at 0, 1 and 6 months. HIV-positive children should receive 3 doses using an adult formulation.

- ***Injecting drug users**

Injecting drug users who have not been infected with hepatitis B should be vaccinated.

- **Recipients of certain blood products**

Screening of all blood donors for HBsAg has greatly decreased the incidence of transfusion-related hepatitis B virus infection. However, patients with clotting disorders who receive blood product concentrates have an elevated risk of hepatitis B virus infection, and should therefore be vaccinated.

- ***Individuals with chronic liver disease and/or hepatitis C**

Hepatitis B vaccination is recommended for those in this category who are seronegative for hepatitis B.[26]

- ***Residents and staff of facilities for people with intellectual disabilities**

Vaccination of carers, staff and susceptible residents is recommended in both residential and non-residential care of people with intellectual disabilities.

- **Individuals adopting children from overseas**

These children should be tested for hepatitis B, and if they are HBsAg positive, members of the adoptive family should be vaccinated.

- ***Liver transplant recipients**

If seronegative for hepatitis B, such individuals should be vaccinated before transplantation as they may be at increased risk of infection from the transplanted organ.

- ***Inmates and staff of long-term correctional facilities**

Inmates are at risk of hepatitis B because of the prevalence of homosexual intercourse, injecting drug use and amateur tattooing in some correctional facilities. Therefore, they should be screened upon incarceration, and vaccinated if susceptible.

- **Healthcare workers, ambulance personnel, dentists, embalmers, tattooists and body-piercers**

The risk to such workers differs considerably from setting to setting in different parts of Australia, but it is recommended that all staff directly involved in patient care,[27] embalming, or in the handling of human blood or tissue, be vaccinated. In addition, standard precautions against exposure to blood or body fluids should be used as a matter of routine.

- **Others at risk**
    - Police, members of the armed forces and emergency services staff should be vaccinated if they are assigned to duties which may involve exposure.
    - Funeral workers and other workers who have regular contact with human tissue, blood or body fluids and/or used needles or syringes.
    - People travelling to regions of intermediate or high endemicity, either long-term or for frequent short terms, should be vaccinated.

- Staff of child day-care centres will normally be at minimal risk of hepatitis B. If advice on risk is sought, the enquiry should be directed to the local public health authority.
- Contact sports generally carry a low risk of hepatitis B infection. Vaccination is nevertheless encouraged.
- As the risk in Australian schools is very low,[28] vaccination of classroom contacts is seldom indicated. Nevertheless, vaccination of all children and adolescents should be encouraged.
- Sex industry workers.

(iv) Serological confirmation of post-vaccination immunity

Post-vaccination serological testing 4 to 8 weeks after completion of the primary course is recommended only for those in the following categories:

- those at significant occupational risk (eg. healthcare workers whose work involves frequent exposure to blood and body fluids),
- those at risk of severe or complicated disease (eg. people with impaired immunity, and individuals with pre-existing liver disease not related to hepatitis B),
- those in whom a poor response to hepatitis B vaccination is expected (eg. haemodialysis patients),
- sexual partners and household contacts of recently notified hepatitis B carriers.[29]

Anti-HBs and HBsAg levels should be measured in infants born to known HBsAg/HBeAg positive carrier mothers 3 to 12 months after completing the primary vaccine course. If anti-HBs levels are adequate and HBsAg is negative, then children are considered to be protected.[29]

(v) Non-responders to primary vaccination

If adequate anti-HBs levels (≥10 mIU/mL) are not reached after the third dose, the possibility of HBsAg carriage should be investigated. Those who are HBsAg negative and do not respond should be offered further doses. These can be given as either a fourth double dose or a further 3 doses at monthly intervals, with further testing at least 4 weeks after the last dose.

There is limited evidence from several trials that HBsAg negative healthcare workers, who are non-responders to a primary course of vaccination and subsequent intramuscular booster schedule, as above, may respond to 5µg of Engerix-B (0.25 mL of the adult formulation) administered intradermally at fortnightly intervals (up to 4 doses) with anti-HBs levels measured before each dose to assess for seroconversion.[30-32] Persistent non-responders should be informed that they are not protected and should minimise exposures, and about the need for HBIG within 72 hours of parenteral exposure to HBV (see Table 3.6.3 *Post-exposure prophylaxis for non-immune individuals exposed to an HBsAg positive person*).

Individuals who are at significant occupational risk who have a documented history of a primary course of hepatitis B vaccine, but it is not known whether they ever seroconverted, and they now have an antiHBs level <10 mIU/mL, should be given a single booster dose of vaccine and have their anti-HBs level checked 4 weeks later. If the anti-HBs level is <10 mIU/mL, regard the individual as a non-responder, give 2 further doses of hepatitis B vaccine at monthly intervals, and re-test for anti-HBs levels at least 4 weeks after the last dose.

(vi) Booster doses

Although vaccine-induced antibody levels decline with time and may become undetectable, booster doses are not recommended in immunocompetent individuals after a primary course, as there is good evidence that a completed primary course of hepatitis B vaccination provides long-lasting protection. This applies to children *and* adults, *including* healthcare workers and dentists.[33-39] However, booster doses are recommended for individuals with impaired immunity, in particular those with either HIV infection or renal failure. The time for boosting in such individuals should be decided by regular monitoring of anti-HBs levels at 6 to 12-monthly intervals.[33]

(vii) Interchangeability of vaccines

Although switching of brands is not recommended, in cases 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 believe that use of a different brand will compromise immunogenicity or safety.

(viii) Post-exposure prophylaxis for hepatitis B

Following significant exposure (percutaneous, ocular, or mucous membrane) to blood or potentially blood-contaminated secretions, the source individual should be tested for HBsAg as soon as possible.

If the person exposed has not been previously vaccinated against hepatitis B, his/her anti-HBs level and HBsAg should be determined immediately. If the person exposed is anti-HBs negative, and the source is either HBsAg positive, or cannot be identified and tested rapidly, administer a single dose of HBIG of 100 IU for children weighing up to 30 kg (about 5 years of age) and 400 IU for all others, within 72 hours. Also give hepatitis B vaccine (by IM injection into either the deltoid or anterolateral thigh, depending on age) as soon as possible, but within 7 days of exposure. Two further doses of vaccine should be given, 1 and 6 months after the first dose.

For previously vaccinated people exposed to either an HBsAg positive source or a source whose hepatitis B status cannot be determined, post-exposure prophylaxis is not necessary if there was a documented protective response (anti-HBs level ≥10 mIU/mL) at any time after vaccination. If the response to previous vaccination is unknown, the anti-HBs level should be determined as quickly as possible. If the anti-HBs level is <10 IU/mL and HBsAg is negative, HBIG and vaccine should be administered as above.

In most instances, it is advisable to offer a course of hepatitis B vaccine to a non-immune healthcare worker sustaining a needle-stick injury or other potential hepatitis B exposure, since the injury or exposure itself is evidence that they work in an area with a significant risk of exposure.

Table 3.6.3: Post-exposure prophylaxis for non-immune individuals exposed to an HBsAg positive person

Type of exposure	Hepatitis B immunoglobulin		Vaccine	
Perinatal (exposure of babies during and after birth)	100 IU by IM injection	Single dose within 12 hours of birth, preferably immediately after birth	0.5 mL by IM injection	Immediately after birth (preferably within 24 hours, no later than 7 days*) then at 2, 4, and either 6 or 12 months of age
Percutaneous/ ocular or mucous membrane	400 IU by IM injection 100 IU if body weight <30 kg	Single dose within 72 hours	0.5 mL or 1 mL by IM injection depending on age	Within 7 days* and at 1 and 6 months after first dose
Sexual	400 IU by IM injection	Single dose within 14 days of sexual contact	0.5 mL or 1mL by IM injection depending on age	Within 14 days* and at 1 and 6 months after first dose

* The first dose can be given at the same time as HBIG, but should be administered at a separate site.

Contraindications

The only absolute contraindications to hepatitis B vaccine are:

- anaphylaxis following a previous dose of hepatitis B vaccine, or
- anaphylaxis following any component of the vaccine.

Adverse events

- Adverse events after hepatitis B vaccination are transient and minor, and include soreness at the injection site (5%, common), fever (usually low grade, 2–3%, common), nausea, dizziness, malaise, myalgia and arthralgia. Fever can be expected in neonates immunised with hepatitis B vaccine (0.6–3.7%, common).
- Anaphylaxis has been reported very rarely in adults. Although various adverse events such as demyelinating diseases, Guillain-Barré syndrome and arthritis have been reported, there is no evidence of a causal relationship with hepatitis B vaccination.[40,41] There have been a few reports of generalised

febrile reactions attributed to yeast allergy, and exceptional instances of polyarteritis nodosa have been reported.

- The World Health Organization Global Advisory Committee on Vaccine Safety states that "multiple studies and review panels have concluded that there is no link between MS [multiple sclerosis] and hepatitis B vaccination".[42]
- The vaccine produces neither therapeutic effects nor adverse events in hepatitis B virus carriers. It is safe in those already immune to hepatitis B.

Use in pregnancy

Refer to Chapter 2.3, *Groups with special vaccination requirements*, Table 2.3.1 *Vaccinations in pregnancy*.

Variations from product information

The product information for both Infanrix hexa and Infanrix Penta states that these vaccines may be given as a booster dose at 18 months of age. NHMRC recommends that a booster dose of DTPa (or DTPa-containing vaccines) is not necessary at 18 month of age. However, DTPa-containing vaccine may be used for catch-up of the primary schedule in children <8 years of age.

Hepatitis B immunoglobulin (HBIG)

Hepatitis B immunoglobulin (HBIG) is prepared from plasma donated through routine blood bank collection. Samples are selected on the basis that they contain high levels of antibody to HBsAg. As stocks of HBIG are very limited, use should be strictly reserved for those who are at high risk, such as babies born to hepatitis B carrier mothers and healthcare workers who are exposed to the blood of HbsAg positive individuals through occupational exposure. Requests should be directed to the Australian Red Cross Blood Service in your State/Territory (see Chapter 3.8, *Immunoglobulin preparations* 'Availability of immunoglobulins').

HBIG is given by IM injection.

- **Hepatitis B Immunoglobulin-VF** – CSL Bioplasma (160 mg/mL immunoglobulin (IgG) prepared from human plasma containing high levels of antibody to surface antigen of the hepatitis B virus). 100 IU and 400 IU ampoules, with the actual volume stated on the label on the vial.

References

Full reference list available on the electronic *Handbook* or website http://immunise.health.gov.au.