

08

Hepatitis A

NOTIFIABLE

In some circumstances, advice in these guidelines may differ from that in the product Summary of Product Characteristics (SmPC). When this occurs, NIAC advises that the recommendations in these guidelines, which are based on current expert advice from NIAC, are followed.

Key Changes

Effects of Hepatitis A

- Prevention

Post-exposure prophylaxis (PEP) recommendations

- Protection of contacts with vaccine

8.1 Introduction

Hepatitis A is an acute, usually mild and self-limiting disease of the liver caused by the hepatitis A virus (HAV). The reservoir of HAV is humans and rarely chimpanzees and other primates. Transmission is almost always by the faeco-oral route. The disease ranges in severity from a mild illness lasting one to two weeks to a severely disabling illness lasting several months. Most patients make a complete recovery. There is no chronic infection. Infection with HAV confers lifelong immunity. Vaccination with two doses induces immunity in almost 100% of recipients; immunity lasts for at least 25 years.

8.2 Epidemiology

Hepatitis A infection is common worldwide. The incidence has been decreasing in better-resourced countries in the past 50 years because of improved hygiene and sanitation. In these countries, disease transmission is most frequent among household and sexual contacts of acute cases. It also occurs sporadically in day-care centres for small children. Outbreaks have been reported frequently in persons who inject drugs (PWID) and in men who have sex with men (MSM). It also occurs among travellers to endemic countries.

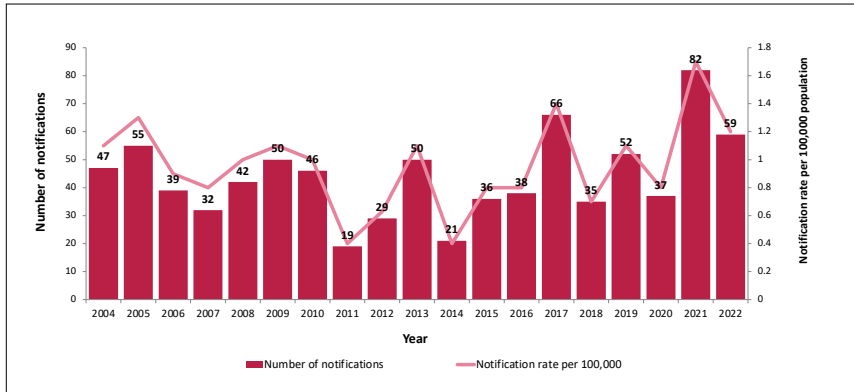
In areas experiencing socio-economic disadvantage where standards of sanitation are poor, HAV infection is common, with infection typically acquired in childhood.

Since 2004, notifications of hepatitis A in Ireland have ranged from 19-82 cases per year (Figure 8.1). The mean number of hepatitis A cases notified annually from 2004-2020, was 41.

The number of hepatitis A notifications more than doubled in 2021 (n=82) compared to 2020 (n=37). This increase was largely driven by two significant outbreaks associated with the Irish traveller community.

Figure 8.1: Number of Hepatitis A notifications, 2004-2022*

Source: HPSC

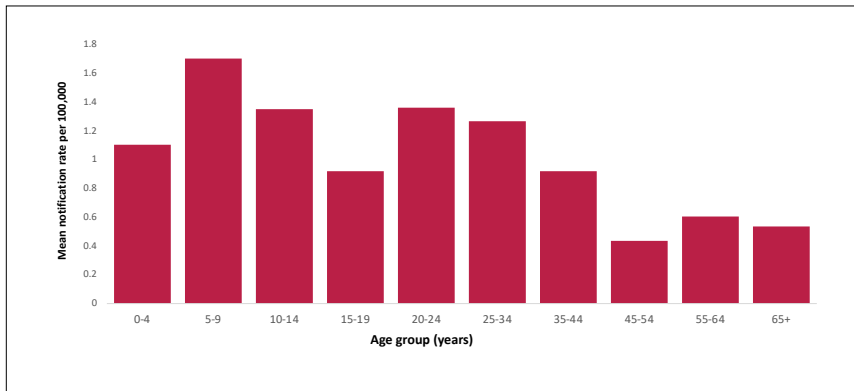


* 2022 data up to 1 December 2022

Figure 8.2 shows the notification rate per 100,000 population by age from 2004-2022. The rates are generally highest in children and young to middle aged adults, reflecting their lack of immunity and travel.

Figure 8.2: Hepatitis A notification rates /100,000 population by age 2004-2022*

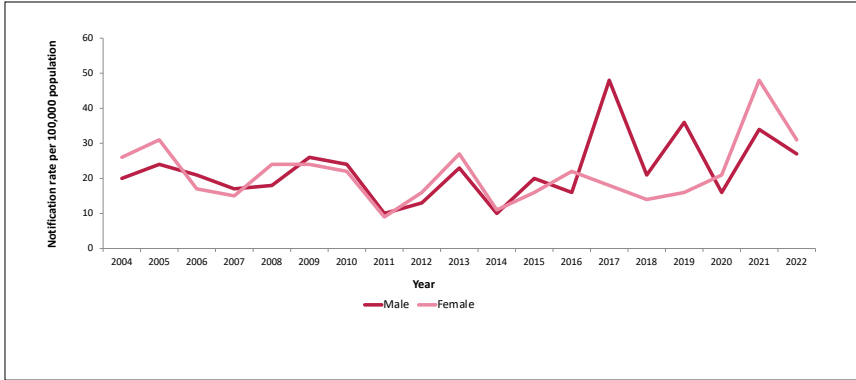
Source: HPSC



*2022 data up to 1 December 2022

Figure 8.3 illustrates the notification rate per 100,000 population by sex from 2004-2022. Rates were generally similar for males and females, except in 2017 when there was a large outbreak in men who have sex with men (MSM). Higher than usual numbers of cases were also identified in MSM in 2018 and 2019. It is likely that most people under the age of 50 in Ireland are susceptible to HAV.

Figure 8.3: Hepatitis A notification rates /100,000 population by sex 2004-2022*
Source HPSC



* 2022 data up to 1 December 2022

8.2.1 Transmission

Person-to-person transmission

HAV infection is spread almost entirely by the faecal-oral route from person to person. Cases are most infectious during the one to two weeks before onset of jaundice; the risk of transmission subsequently decreases and is minimal by one week after the onset of jaundice **or** two weeks after the onset of prodromal symptoms if jaundice does not occur.

Faecal viral shedding may continue for several months in infants and children, in the immunosuppressed, and in those with prolonged cholestasis or relapsing illness. Faecal shedding and viraemia have been reported to persist for longer than previously recognised in immunocompetent patients. It is important to advise patients to exercise good hygiene, even after the apparent infectious period is over.

The risk of faecal-oral transmission is increased where there is close person-to-person contact, e.g. among infants, young children, and those with learning disability, especially in day-care and residential homes. The risk is also increased where there is socio-economic disadvantage, and where poor hygiene standards prevail. Because most children (50-90%) have asymptomatic or unrecognised infection but shed virus in their faeces, they play an important role in HAV transmission.

HAV may be transmitted by sexual oral-anal contact or oropharyngeal secretions.

HAV is transmitted mainly by the faecal-oral route. Infected persons are most likely to transmit the virus one to two weeks before the onset of illness.

Food and water contamination

Contamination of water supplies with HAV- infected faeces occurs where sewage disposal is inadequate. Transmission may occur after ingestion of food washed in contaminated water or handled by an infected person with poor standards of hygiene. It may also occur following ingestion of food not further cooked after being contaminated, or of shellfish harvested from contaminated seawater.

Intravenous transmission

A transient viraemia occurs during HAV infection. However, outbreaks of hepatitis A have rarely been linked to blood and blood product administration. Persons who inject drugs (PWID) are at increased risk, probably due to a combination of factors, including poor standards of hygiene. Percutaneous transmission, as a result of contamination of drugs and needle- sharing may also contribute.

8.3 Effects of hepatitis A

The incubation period for HAV averages 28 days (range 15-50 days). Within 10-12 days of infection the virus is present in the blood and is excreted into the faeces via the biliary tract. The viral load is higher in faeces than in blood.

In children less than six years of age, most (90%) infections are asymptomatic. The frequency and severity of symptoms increase with age, with jaundice occurring in 70-95% of infected adults. The illness usually lasts up to two months, and is characterised by fever, malaise, myalgia, anorexia, nausea and jaundice. Diarrhoea is more common in children. Ten to 15% have prolonged or relapsing signs and symptoms for up to six months. Chronic liver damage, fulminant hepatitis, hepatic coma and death can occur but are rare. The overall case fatality rate is low.

Older persons, the immunosuppressed, people with chronic liver disease, liver transplant recipients, and those with chronic hepatitis B and C infection are more likely to have severe manifestations of HAV infection. Case fatality rates can reach 2% for adults over 50 years of age.

8.3.1 Prevention

Safe sanitation and good hygiene practices, particularly hand washing, are the cornerstone of prevention and should be promoted, especially in settings and communities with higher rates or at increased risk of infection. A selective vaccination policy is of benefit for those at increased risk of infection (section 8.5 and 8.6.1).

8.4 Hepatitis A vaccines

Hepatitis A vaccines are non-live and cannot cause the disease against which they protect. They are not licensed for use in children less than one year of age. They may be used in pregnancy, depending on a benefit-risk assessment.

8.4.1 Hepatitis A vaccines are available as either monovalent vaccine or combined with hepatitis B or typhoid vaccines.

Monovalent vaccine

Hepatitis A vaccine: inactivated HAV grown in human diploid cells and adsorbed onto aluminium.

Approximately 95% of subjects acquire protective levels of HAV antibodies within four weeks of one dose and over 99% after the second dose. Immunocompetent subjects show a satisfactory antibody response up to three years after the first dose of Avaxim[®] and up to five years after the first dose of Havrix Monodose[®] and Havrix Paediatric[®]. The duration of the immune response after two doses is at least 25 years. It is likely that at least 95% and 90% of subjects will remain seropositive 30 and 40 years after vaccination, respectively.

Licensed indications: active immunisation against hepatitis A of children from one year of age and adults.

Combined hepatitis A and hepatitis B (HBV) vaccine

A combined vaccine containing purified inactivated HAV and purified recombinant hepatitis B surface antigen (HBsAg) adsorbed onto aluminium may be used when protection against both HAV and HBV is required.

Combined HAV and typhoid vaccine

A combined vaccine containing purified inactivated HAV and purified Vi polysaccharide typhoid vaccine may be used where protection against HAV and typhoid fever is required (see Chapter 5).

A full list of Hepatitis A-containing vaccines is shown in Table 8.1.

Table 8.1. Hepatitis A vaccines - dose and antigen content

Vaccine	Age (years)	Dose	Antigen content(s)	
			Hepatitis A	Other
Avaxim®	16 and older	0.5ml	160EU ¹	
Havrix Monodose®*	16 and older	1ml	1440EU	
Havrix Paediatric®*	1 to 15	0.5ml	720EU	
Twinrix Adult®	16 and older	1ml	720EU	Hepatitis B 20mcg
Viatim®	16 and older	1ml	160U ²	Typhoid 25mcg Ty2 polysaccharide

¹ ELISA Unit. In the absence of an international standardised reference, the antigen content is expressed using an in house reference from the manufacturer.

² Units measured using an in-house method of the manufacturer.

***Those at high medical risk should only be given monovalent hepatitis A vaccine.**

In the absence of a supply of monovalent paediatric hepatitis A vaccine a 1ml (full dose) of adult hepatitis A vaccine should be given to any child aged 1 to 15 years requiring post exposure prophylaxis. This may be given in two divided doses at the same visit to children age 1 to 2 years.

HAV containing vaccines should be stored at +2 to +8°C and should be protected from light.

An up-to-date list of licensed and marketed vaccines can be accessed on the HPRA website www.hpra.ie

A list of the vaccines currently available from the National Cold Chain Service can be accessed at www.immunisation.ie

8.4.2 Dose and route of administration

Monovalent Hepatitis A vaccine

Two doses IM, 6 -12 months apart.

The product used for the second dose (Avaxim, Havrix Monodose or Havrix Paediatric) should be based on age at the time of that dose (Table 8.1).

If the second dose is delayed, the course does not need to be repeated.

Current data do not support the need for further booster vaccination of immunocompetent subjects after a two dose vaccination course.

Combined Hepatitis A and Hepatitis B vaccines

Twinrix Adult®

Three doses of 1ml IM at 0, 1, and 6 months.

In exceptional circumstances in adults, when travel is anticipated within one month or more after initiating the vaccination course, but where insufficient time is available to allow the standard 0, 1, 6 month schedule to be completed, a schedule of three IM doses at 0, 7 and 21 days may be used. When this schedule is applied, a fourth dose is recommended 12 months after the first dose.

Booster dose

Long-term antibody persistence data following vaccination with Twinrix Adult are available up to 15 years after vaccination. The anti-HBs and anti-HAV antibody titres observed following a primary vaccination course with the combined vaccine are in the range of what is seen following vaccination with the monovalent vaccines. The rates of antibody decline are also similar. General guidelines for booster vaccination can therefore be drawn from experience with the monovalent vaccines.

Booster vaccination is unlikely to be necessary for at least 25 years.

Combined Hepatitis A/Typhoid vaccines

Two 1ml doses 6-12 months apart.

8.5 Pre-exposure prophylaxis recommendations

Immunisation with hepatitis A vaccine is recommended for the following non-immune persons:

- Those aged one year or older travelling to or living in countries where hepatitis A is common (all countries of the world except Western Europe, Australia, New Zealand, Canada, the United States, Japan, the Republic of Korea, and Singapore)

- Persons with chronic hepatitis B or C infection
- Persons with chronic liver disease or awaiting liver transplant
- Recipients of plasma-derived clotting factors (e.g. those with haemophilia)
- Persons who inject drugs (PWID)
- Men who have sex with men (MSM)
- Those who have multiple anonymous sex contacts
- Food handlers
- Carers of, or persons with developmental disabilities
- Laboratory staff who may be exposed to HAV in the course of their work.
- Workers exposed to raw untreated sewage
- Staff who work with non-human primates that are susceptible to hepatitis A infection
- Household members and close personal contacts of adopted children newly arriving from countries with high or intermediate hepatitis A endemicity (see first bullet). Immunisation should preferably be offered before adoption.

For those aged over 50 years or with a history of jaundice, haemophilia or residence in a high-risk area, pre-vaccination testing for immunity to hepatitis A may be considered in order to reduce costs. Post-vaccination testing for anti-HAV is not indicated.

In the case of patients on immunomodulatory/immunosuppressive treatment, an additional priming dose pre-travel should be considered. This can be administered in two sites on the same day or a further dose one month later, time permitting. This leads to a significantly increased protective effect. *This does not complete the course, and a booster dose should be administered six to twelve months later.*

Vaccination should be carried out three or more weeks before departure. However, if the time before departure is short, the vaccine is still likely to prevent or modify the infection (Chapter 5). HNIG may be used for travellers who are immunocompromised and should be given at a separate site to the vaccine

Contraindications

Anaphylaxis to any of the vaccine constituents.

Precautions

Acute severe febrile illness; defer until recovery.

All monocomponent Hepatitis A vaccines contain phenylalanine, which may be harmful to patients that have phenylketonuria (PKU).

Pregnancy

HAV containing vaccines may be given to pregnant women if clinically indicated. Safety data in pregnant women are not available, but the risk is considered to be low or non-existent because the vaccines contain inactivated purified viral proteins.

Adverse reactions

Local: very common: soreness, erythema and induration at the injection site.

General: common: fever, malaise, fatigue, headache, nausea, loss of appetite.

8.6 Post-exposure prophylaxis (PEP) recommendations

8.6.1 Protection of contacts with vaccine (See [Figure 8.4](#))

Hepatitis A vaccine is recommended for the management of contacts of cases and for outbreak control.

i. Close personal contacts

- children aged one year or older* and adults living in the same household as the index case or regularly sharing food or toilet facilities with the index case during the infectious period; this includes family and friends who frequently visit the household (a large number of people may fit into this category for Irish Travellers or other nomadic communities).
- children aged one year and older* and adult carers in contact with the index case in a child-care centre. Risk assessment should consider the size of the centre, the age profile (in particular the numbers in nappies) and intermixing of different age groups and carers.
- persons who have had sexual contact with the index case during the infectious period.
- persons who have shared syringes with an index case and who are in an at risk group (Section 8.6.2) should receive hepatitis A vaccine, or HNIG and hepatitis A vaccine simultaneously.

*If vaccination of carers is not feasible, vaccinate children from two months of age.

ii. **Outbreaks**

Vaccination is not normally indicated when a single case occurs in a school, workplace, hospital, prison or other congregate setting. Instead careful hygiene practices should be emphasised.

In a school setting, parents of children in the same class should be informed of the risk of possible exposure.

Vaccination should be offered to persons who have close contact with the index case if epidemiological investigation indicates HAV transmission has occurred in a school, workplace, hospital, prison or other congregate setting.

In conjunction with prevention strategies ([Section 8.3.1](#)), vaccination may be effective in outbreaks to interrupt onward transmission in settings such as Irish Traveller sites, other nomadic populations, homeless outreach shelters or hostels.

Food or waterborne outbreaks

If a food handler is the index case, vaccination should be offered to other food handlers at the same location, if the risk of transmission is high.

Vaccination of patrons should only be considered if:

- a. during the time the food handler was likely to be infectious, s/he had handled uncooked or cooked food and had diarrhoea or bad hygiene practices
- and*
- b. patrons can be identified and treated within two weeks of exposure.

Hepatitis A vaccine is recommended for persons aged 1 to 59 years, *who are within two weeks of exposure* and who have no previous history of hepatitis A vaccine or of laboratory confirmed hepatitis A infection.

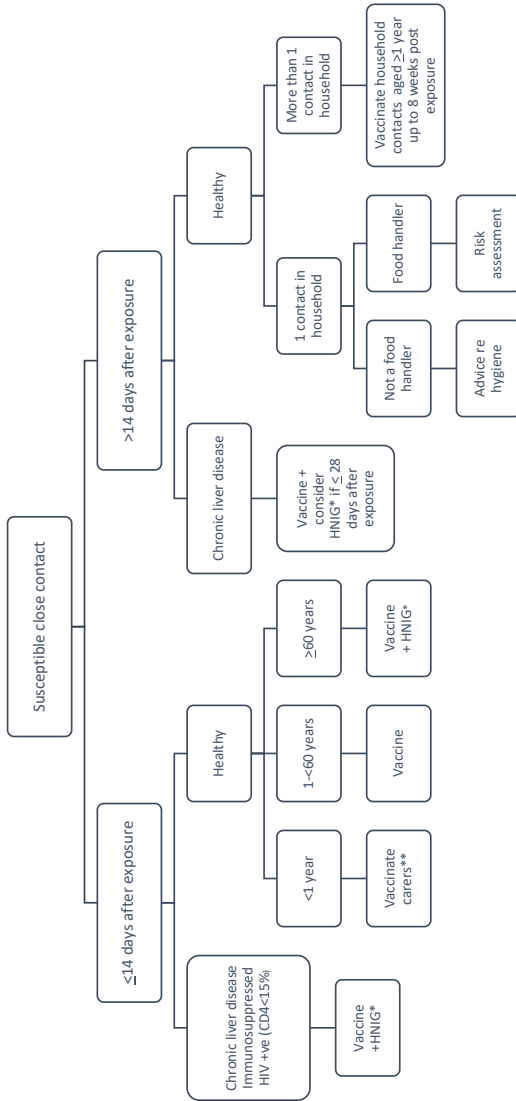
Monovalent hepatitis A vaccine is the preferred vaccine for post- exposure prophylaxis.

Chapter 8 Hepatitis A

In shared households with more than one close contact, hepatitis A vaccine should be offered to all contacts seen *within eight weeks of exposure* to prevent tertiary cases within the household.

Havrix Monodose® should be used if rapid protection is required, as it contains higher amounts of hepatitis A antigen and provides protection more quickly than combination hepatitis A and B vaccines.

Figure 8.4. Management of susceptible close contacts of Hepatitis A



* Anti HAV IgG testing prior to HNIG if feasible

** If not feasible, vaccinate those > 2 months of age

8.6.2 Protection of contacts with immunoglobulin

Human normal immunoglobulin (HNIG) may be indicated **in addition to vaccine** for those in the groups below, because of lack of information regarding vaccine efficacy and more severe manifestations of hepatitis A:

- persons aged 60 years and older
- those aged one year or older at risk of severe complications (e.g. those with chronic liver disease, including chronic hepatitis B or C infection)
- those immunosuppressed by disease or treatment.

HNIG is more than 85% effective in preventing symptomatic infection when administered within two weeks after exposure to HAV.

For those with chronic liver disease, consider HNIG up to four weeks after exposure, as it may modify the disease.

If contacts are at ongoing risk of HAV infection they should be offered vaccine irrespective of whether they are offered HNIG.

Serological testing of the contacts is usually not recommended as it may result in unnecessary delay in the administration of prophylaxis.

Vaccine and HNIG may be given at the same time, but in different sites, when both rapid and prolonged protection is required.

HNIG can interfere with the response to live virus vaccines (Chapter 2).

8.7 HNIG preparations, dose and administration

There is no HAV-specific IG product available for use in Ireland. Although HNIG products are not licensed for post exposure prophylaxis, their use has proven effective in preventing or attenuating Hepatitis A. Most national guidelines on HAV PEP quote an effectiveness of 80-90% for the use of IG against HAV infection, if administered within 14 days post-exposure.

Because of the changing epidemiology of HAV in high-resource countries, there has been a decline in anti-HAV concentrations in IG products. The anti-HAV concentration in HNIG available for HAV PEP in Ireland is unknown.

HNIG should be given to vulnerable contacts as soon as possible after exposure, ideally within 14 days. There is no consistent evidence regarding the efficacy of immunoglobulin received 14 days or more after exposure, and its use is primarily to reduce the severity of disease in vulnerable contacts.

HNIG is recommended for vulnerable contacts who are within two weeks of exposure and have no previous history of hepatitis A vaccine or laboratory confirmed hepatitis A infection

8.7.1 Preparations

Four HNIG products are licensed and available in Ireland for subcutaneous (SC) administration - **Cuvitru**[®] (20%), **Gammanorm**[®] (16.5%), **Hizentra**[®] (20%) and **Subcuvia**[®] (16%).

Following SC administration, peak serum IgG levels are reached by Hizentra[®] in approximately two days, by Cuvitru[®] in 3 days, by Subcuvia[®] in 4-5 days, and by Gammanorm[®] in 4-6 days.

Cuvitru[®] or Hizentra[®] are recommended, because of the smaller volume required, and the earlier peak serum levels achieved compared to lower concentration products.

8.7.2 Dose and administration

Cuvitru and Hizentra 200mgs/ml (1g/5mls) The product should be administered via the subcutaneous route. The following is given as a guideline.

Dose: 0.2 to 0.5 g/kg (1 to 2.5 ml/kg) body weight, depending on a risk assessment.

Always consult the SmPC for information about product usage, dose, administration, and adverse events

If SC/IM HNIG is not available, in certain high-risk situations IVIG can be substituted.

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Chapter 8 Hepatitis A

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