

08

Hepatitis A

NOTIFIABLE

In some circumstances, advice in these guidelines may differ from that in the Summary of Product Characteristics of the vaccines. When this occurs, the recommendations in these guidelines, which are based on current expert advice from NIAC, should be followed.

Introduction

Hepatitis A is an acute, usually mild and self-limiting disease of the liver caused by the hepatitis A virus (HAV). The disease varies in clinical severity from a mild illness lasting 1-2 weeks to a severely disabling disease lasting several months. Most patients make a complete recovery. HAV hepatitis does not progress to chronic liver disease and there is no chronic carrier state. On rare occasions the disease may be very severe, with fulminant hepatitis, liver coma and death.

Severity of illness is strongly age dependent with most young children remaining asymptomatic. Case fatality can reach 2% for adults over 50 years of age. Persons with pre-existing chronic liver disease have an increased risk of death from fulminant hepatitis A. Infection with HAV confers life-long immunity.

Epidemiology

Hepatitis A infection is common worldwide. The incidence of hepatitis A 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 occurs sporadically in day-care centres with small children. It also occurs among travellers to endemic countries. Outbreaks have been reported

frequently in injecting drug users and in men who have sex with men. In low resource countries where standards of sanitation are poor, HAV infection is common and occurs in early life.

The incidence of hepatitis A in Ireland has fallen substantially since 2000, with fewer than 50 cases now being notified per year (Figure 8.1). The crude notification rate in 2011 was 0.4 per 100,000 population. The significant reduction in notifications since 2001 most likely reflects improved living conditions, as HAV seroprevalence rates are strongly correlated with socioeconomic status and access to clean water and sanitation.

Figure 8.1: Number of Hepatitis A notifications, 1995-2012

Source HPSC

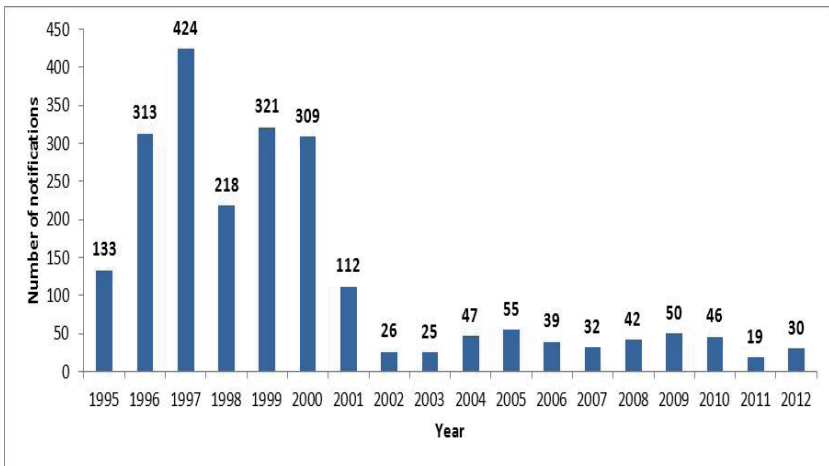
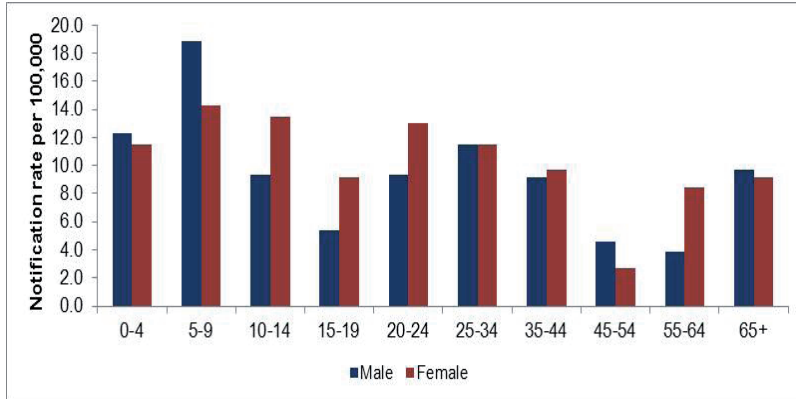


Figure 8.2 illustrates the age and sex-specific cumulative notification rate per 100,000 population from 2002 to 2012. It is likely that most people under the age of 50 in Ireland are susceptible to HAV.

Figure 8.2: Age and sex specific cumulative notification rates/100,000 population for hepatitis A 2002 – 2012

Source CIDR HPSC



Transmission

Person-to-person transmission

HAV infection is spread primarily by the faecal-oral route from person to person. Cases are most infectious during the 1 to 2 weeks before onset of jaundice and the risk of transmission subsequently decreases and is minimal by 1 week after onset of illness.

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 overcrowding and where poor hygiene standards prevail. Because most children have asymptomatic or unrecognised infections, they play an important role in HAV transmission and serve as a source of infection for others.

Sexual transmission: HAV may be transmitted by sexual oral-anal contact or by oropharyngeal secretions. There is an association with multiple anonymous sexual contacts.

HAV is transmitted by the faecal-oral route. Infected persons are most likely to transmit HAV 1-2 weeks before the onset of illness.

Less common modes of transmission

Food and water contamination

Contamination of water supplies with infected faeces occurs where sewage disposal is inadequate. Food washed in contaminated water or prepared by an infected person with poor standards of hygiene may cause viral transmission and infection. Shellfish harvested from contaminated sea water may also cause HAV outbreaks.

Intravenous transmission

A viraemia occurs briefly during HAV infection. Outbreaks of hepatitis A have rarely been linked to blood and blood product administration. The observed increased incidence of infection among injecting drug users is probably due to poor standards of hygiene, although contamination of drugs and needle-sharing may contribute.

Effects of hepatitis A

The incubation period for HAV is approximately 28-30 days, with a range of 15-50 days. After 10-12 days the virus is present in the blood and is excreted into the faeces via the biliary tract. The virus is present in the blood but the viral load is much higher in the faeces.

In children under 6 years of age, most (70%) infections are asymptomatic. The frequency and severity of symptoms increase with age, with jaundice occurring in 70% of infected adults. The illness usually lasts up to 2 months, characterised by fever, malaise, anorexia, nausea and jaundice, although 10-15% have prolonged or relapsing signs and symptoms for up to 6 months. There is no chronic carrier state and chronic liver damage is rare. Fulminant hepatitis can occur but is rare.

Prevention

Good hygiene, particularly hand washing, is the cornerstone of prevention and should be promoted in settings and communities with higher rates or risk of infection. A selective vaccination policy is of benefit for certain groups with greater likelihood of infection.

Hepatitis A vaccine

Hepatitis A vaccines are inactivated, do not contain live organisms and cannot cause the disease against which they protect. They have been shown to be safe, immunogenic and efficacious. The vaccines are not licensed for use in children less than 1 year of age and are not recommended by the manufacturers for use in pregnancy. The risk associated with vaccination

should be weighed against the risk for hepatitis A in pregnant women who might be at high risk for exposure to HAV.

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

Monovalent vaccines

Hepatitis A vaccine is formaldehyde inactivated vaccine prepared from hepatitis A virus grown in human diploid cells (MRC5) and adsorbed onto an aluminium hydroxide adjuvant. Approximately 95% of subjects acquire protective levels of HAV antibodies within 4 weeks of one dose, and over 99% after the second dose. The duration of the vaccine induced immune response has been demonstrated to protect for at least 15 years. It is likely that at least 95% and 90% of subjects will remain seropositive (>15 mIU/ml) 30 and 40 years after vaccination, respectively.

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 hydroxide (HAV) aluminium phosphate (HBV) may be used when protection against both HAV and HBV is required.

Adult Hepatitis A (or combined Hepatitis A/ Hepatitis B) vaccine is recommended for those aged 16 and older and paediatric Hepatitis A (or combined Hepatitis A/ Hepatitis B) vaccine for those aged 1 to <16 years.

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).

An up-to-date list of licensed 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 found at www.immunisation.ie

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

Dose and route of administration

The schedule for monovalent Hepatitis A (and combined Hepatitis A and typhoid) vaccines is a single dose of 0.5 or 1ml followed by a booster at 6-12 months.

The schedule for combined Hepatitis A and Hepatitis B vaccine depends upon the product.

The schedule for Twinrix consists of three doses of 0.5mls, the initial dose followed by a second dose at one month and a third six months after the first dose.

For Ambirix the schedule consists of two doses, the initial dose followed by a second dose between 6 and 12 months after the first dose.

Hepatitis A vaccine should be given by intramuscular injection in the anterolateral thigh or deltoid region.

Indications

PRE-EXPOSURE PROPHYLAXIS

Immunisation with hepatitis A vaccine is recommended for:

- Travellers, including children 1 year and over, to areas with high or intermediate hepatitis A endemicity (Africa, Asia, Central and South America, Eastern Europe, the Middle East). Vaccination should be carried out 2 or more weeks before departure. However, if the time before departure is short, the vaccine is still considered likely to prevent or at least modify the infection (see Chapter 5). HNIG could be used (if available) for travellers who are immunocompromised and should be given at a separate site.
- Non-immune patients with chronic hepatitis B or chronic hepatitis C infection.
- Non-immune individuals with chronic liver disease and those awaiting liver transplant.
- Persons with haemophilia and other recipients of plasma-derived clotting factors.
- Injecting drug users.
- Men who have sex with men.
- Clients of learning disability services whose capacity to maintain good standards of hygiene is limited, and their carers.
- Laboratory workers who may be exposed to HAV in the course of their work.

- Workers exposed to raw untreated sewage.
- Susceptible staff who work with non-human primates that are susceptible to hepatitis A infection.
- Household members and other 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.

Contraindications

Anaphylaxis to any of the vaccine constituents.

Individuals who have had a confirmed anaphylactic hypersensitivity to egg products should not be given the hepatitis A vaccine Epaxal, as a component of that vaccine is prepared on hens' eggs.

Precautions

Acute severe febrile illness, defer until recovery.

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: Reactions of soreness, erythema and induration at the injection site are very common.

General: Symptoms such as fever, malaise, fatigue, headache, nausea and loss of appetite occur less frequently.

POST-EXPOSURE PROPHYLAXIS

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

Hepatitis A vaccine is recommended for persons aged 1 to 50 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 generally the preferred vaccine for post-exposure prophylaxis. However, in children under 16 years, a single dose of

Ambirix may be used for rapid protection against hepatitis A. Both Ambirix and monovalent vaccines contain higher amounts of hepatitis A antigen and provide hepatitis A protection more quickly than Twinrix.

Protection of contacts with immunoglobulin

Human normal immunoglobulin (HNIG) may be indicated in addition to, or instead of, vaccine in limited circumstances as described below. HNIG is greater than 85% effective in preventing symptomatic infection when administered within 2 weeks after exposure to HAV.

Indications

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

- persons aged over 50 years
- those aged 12 months and older at risk of severe complications (those with chronic liver disease, including chronic hepatitis B or C infection).

HNIG is recommended in the groups above because of the absence of information regarding vaccine performance and the more severe manifestations of hepatitis A.

In general the use of HNIG more than 2 weeks after the last exposure is not indicated.

For children under 12 months of age, no intervention for the child is recommended. However, vaccine should be offered to non-immune carers (to prevent tertiary infection) and consideration given, in consultation with the Department of Public Health, to exclusion of the child from childcare.

If contacts are at ongoing risk of HAV infection because of their lifestyle or for any other reason, they should be offered vaccine irrespective of whether they are offered HNIG.

Serological testing of the contacts may be performed, but 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.

- *Child-care centre staff, children, and their household contacts.*

If one or more hepatitis A cases are associated with a centre, immunoprophylaxis (as above) should be offered to the children and the adult carer(s) in contact with the index case. The need for prophylaxis for a wider group of carers and children should be based upon risk assessment.

The risk assessment should consider the size of the centre, the age profile (in particular the numbers in nappies), and mixing of the different age groups and carers. When an outbreak occurs (i.e. hepatitis cases in 2 or more households) immunoprophylaxis should also be considered for members of households that have children (centre attendees) in nappies. No specific intervention is recommended for children under 12 months of age.

- *Schools, hospitals, prisons and work settings.*

Immunoprophylaxis is not normally indicated when a single case occurs in a school, office or other work-setting. Instead, the importance of 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. Immunoprophylaxis as above should be offered to persons who have close contact with index patients if an epidemiological investigation indicates HAV transmission has occurred in this setting.

- *Food or waterborne outbreaks.*

If a food handler is diagnosed with hepatitis A, immunoprophylaxis should be offered to other food handlers at the same location, if the risk of transmission is high. Administration of immunoprophylaxis to patrons should only be considered if: (1) during the time the food handler was likely to be infectious, the food handler had both directly handled uncooked foods or foods after cooking and had diarrhoea or bad hygiene practices and (2) patrons can be identified and treated within two weeks of exposure.

- *Close personal contact.*

Immunoprophylaxis should be offered to previously unvaccinated household or sexual contacts of cases of recent HAV infection.

Those who have shared syringes with a person who has serologically confirmed hepatitis A should receive hepatitis A vaccine, or HNIG and hepatitis A vaccine simultaneously.

HNIG can interfere with the response to live virus vaccines (see Chapter 2 for more information on HNIG).

Subgam, the HNIG product, is available in Ireland for Hepatitis A prophylaxis. It is unlicensed for this indication, as Hepatitis A antibody levels in Subgam are below the recommended WHO standard of 100IU/ml. As a result, the dose required to prevent or modify hepatitis A infection is higher than for previous products. The recommended dose of Subgam to provide levels of antibody equivalent to that achieved with products meeting the WHO standard is:

<10 years	500 mg* by intramuscular injection
≥10 years	750 mg* by intramuscular injection

*Subgam is presented as three vial sizes of 250mg, 750mg, and 1500mg of protein

Bibliography

Department of Health, UK (2013). Immunisation against Infectious Diseases (The Green Book) www.dh.gov.uk/greenbook

HPSC (2012). HPSC Annual Report 2011
<http://www.hpsc.ie/hpsc/AboutHPSC/AnnualReports/File,13847,en.pdf>

Victor JC, Monto AS, Surdina TY, Suleimenova SZ, Vaughan G, Nainan OV, Favorov MO, Margolis HS and Bell BP (2007). Hepatitis A Vaccine versus Immune Globulin for Postexposure Prophylaxis. *NEJM*; 357(17): 1685-94.

WHO position paper on hepatitis A vaccine (2012). *WER*. 87, 261-276.