

05

Hepatitis A

NOTIFIABLE

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.

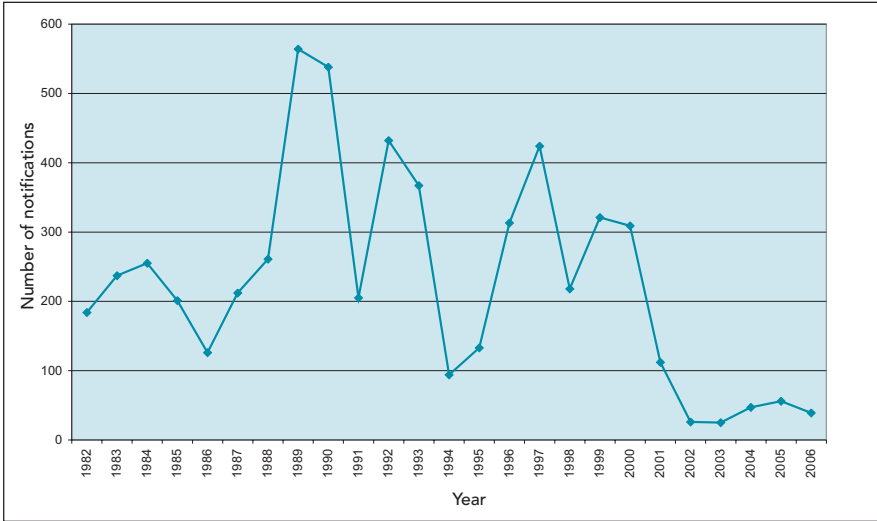
Severity of illness increases with age. Case fatality can reach 2% for adults over 50 years of age. Persons with pre-existing chronic liver disease have an elevated risk of death from fulminant hepatitis A. Infection confers life-long immunity.

Epidemiology

Hepatitis A infection is common worldwide. The incidence of hepatitis A has been decreasing in developed countries over the past 50 years because of improved hygiene and sanitary conditions. 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 the developing world 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 2002, with fewer than 60 cases notified per year (Figure 5.1). The age-standardised incidence rate in 2005 was 1.4 per 100,000 population. It is likely that most people under the age of 50 in Ireland are now susceptible to HAV.

Figure 5.1 Number of hepatitis A notifications in Ireland, 1982-2006.
Source: HPSC



Transmission

Person-to-person transmission

HAV infection is spread primarily by the faecal-oral route from person to person.

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.

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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.

Percutaneous-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 intravenous 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, 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

HAV vaccines have been shown to be safe, immunogenic and efficacious. The vaccines are not licensed for use in children under 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. HAV vaccines are available as either monovalent vaccines, or combined with either typhoid or hepatitis B vaccines.

Monovalent vaccines

HAV vaccine is a formaldehyde inactivated vaccine prepared from hepatitis A virus grown in human diploid cells (MRC5) and adsorbed onto an aluminium hydroxide adjuvant. The vaccine should be stored at 2-8°C and should be protected from light.

The primary course of HAV vaccine is a single dose followed by a booster at 6-12 months. Approximately 95% of subjects acquire protective levels of HAV antibodies within 4 weeks of one dose, and over 99% after the second dose. It is expected that immunity for at least 20 years is conferred by the full course.

Combined hepatitis A and hepatitis B (HBV) vaccine

A combined vaccine containing purified inactivated HAV virus and purified recombinant HBsAg 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.

Route of administration

Hepatitis A vaccine should be given intramuscularly in the deltoid region. For patients with severe bleeding tendencies (e.g. persons with haemophilia), subcutaneous injection may be considered. Hepatitis A vaccine should not be administered intravenously.

Indications

Pre-exposure prophylaxis

Active 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 19). HNIG could be used (if available) for travellers who are immunocompromised and should be given at a separate site
- Susceptible persons with chronic liver disease
- Non-immune patients with chronic hepatitis B or hepatitis C infection
- Solid organ transplant recipients who have not been immunised previously – should be immunised prior to transplantation
- 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
- Sewage 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 with recent close contact with infected individuals, see *Post-exposure prophylaxis, below*.

Where indicated, HAV vaccination can be combined with HBV vaccination.

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

Contraindications

Anaphylactic reaction to a preceding dose or any of the 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. 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

Side effects are infrequent and mild.

Post-exposure prophylaxis

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

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immunoglobulin (HNIG) may be indicated in addition to, or instead of, vaccine in limited circumstances as described below. Immunoprophylaxis should be given to household and close contacts of cases that have no previous history of hepatitis A vaccine or of laboratory confirmed hepatitis A infection as soon as possible after exposure to HAV.

Following the publication of recent data comparing the efficacy of hepatitis A vaccine and HNIG after exposure to HAV, HAV vaccine is now 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.

For persons aged 51 years and over and those with underlying medical conditions, who are within two weeks of exposure and who have no previous history of hepatitis A vaccine, or of laboratory confirmed hepatitis A infection, HNIG (if available) is recommended in addition to vaccine, because of the absence of information regarding vaccine performance, and the more severe manifestations of hepatitis A in these groups.

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 conjunction with the local office of public health – to exclusion of the child from childcare.

In general the use of HNIG more than 2 weeks after the last exposure is not indicated. However, if HNIG is given after 2 weeks from last exposure it may modify disease severity and may be offered to those 51 years of age and over and those at risk of severe complications (those with chronic liver disease, including chronic hepatitis B or C infection).

Monovalent hepatitis A vaccine is the preferred vaccine for post exposure prophylaxis as no data exists regarding the performance of the combination vaccine for prophylaxis after exposure to HAV. If a contact is 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.

Subgam® 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 dosage 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

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. If the centre admits children in nappies, immunoprophylaxis should be offered to all children and staff in the centre. Where HAV infection is confirmed in 2 or more households of children attending such a centre, immunoprophylaxis should similarly be offered to all children and staff. In centres that do not provide care to children in nappies, hepatitis A vaccine or HNIG need be administered only to classroom contacts of the index patient. When an outbreak occurs (i.e. hepatitis cases in 3 or more families) immunoprophylaxis should also be considered for members of households that have children 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 persons with serologically confirmed recent HAV infection.

In addition, people who have shared illicit drugs with a person who has serologically confirmed hepatitis A should receive hepatitis A vaccine, or HNIG and hepatitis A vaccine simultaneously. People at continued risk of infection should be advised to receive a second dose of vaccine at 6-12 months after the first dose.

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

Bibliography

CDC (2006). Prevention of hepatitis A through active or passive immunization. Recommendation of the Advisory Committee on Immunization Practices (ACIP). MMWR; 55 (No. RR-7);1-23.

Crowcroft NS, Walsh B, Davison KL, Gungabissoon U on behalf of PHLS Advisory Committee on Vaccination and Immunisation (2001). Guidelines for the control of hepatitis A virus infection. *Commun Dis Public Health*; 4:213-27.

Hawker J, Begg N, Blair I, Reintjes R, Weinberg J (2005). *Communicable Disease Control Handbook*. 2nd ed. Massachusetts: Blackwell Publishing.

Health Protection Surveillance Centre (2006). Annual report 2005. Available from: www.ndsc.ie/hpsc/AboutHPSC/AnnualReports/

Heymann D, editor (2004). *Control of Communicable Diseases Manual*. 18th ed. Washington: APHA.

Kumar P, Clark M, editors (2005). *Clinical Medicine*. 6th ed. Edinburgh: Elsevier Saunders.

Salisbury D, Ramsay M, Noakes K, editors (2006). *Immunisation against infectious disease*. London: Department of Health.

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.