17 Hepatitis A

17.1 Introduction

17.1.1 Hepatitis A is transmitted by the faecal-oral route. Person to person spread is the most common method of transmission although contaminated food or drink may sometimes be involved. The incubation period is about 15-40 days and the disease is generally mild. Asymptomatic disease is common in children and severity tends to increase with age. Occasional cases of fulminant hepatitis may occur but there is no chronic carrier state and little likelihood of chronic liver damage.

17.1.2 The incidence of hepatitis A shows a cyclical pattern in the UK, the most recent peak year being 1990 when 7,545 cases were reported to the Public Health Laboratory Service from England and Wales. As of 30 June 1996, there were 1,750 reports in 1995. Over 80% of cases are contracted in the UK and, whilst the majority of these are sporadic, outbreaks do occur.

17.1.3 The prevalence of hepatitis A in countries outside Northern and Western Europe, North America, Australia and New Zealand is higher than in the UK. In 1995 approximately 220 (13%) of the cases notified to PHLS included a history of travel abroad in the six weeks before the onset of illness. The highest risk areas are the Indian subcontinent and the Far East, but the risk extends to Eastern Europe.

17.2 Vaccine

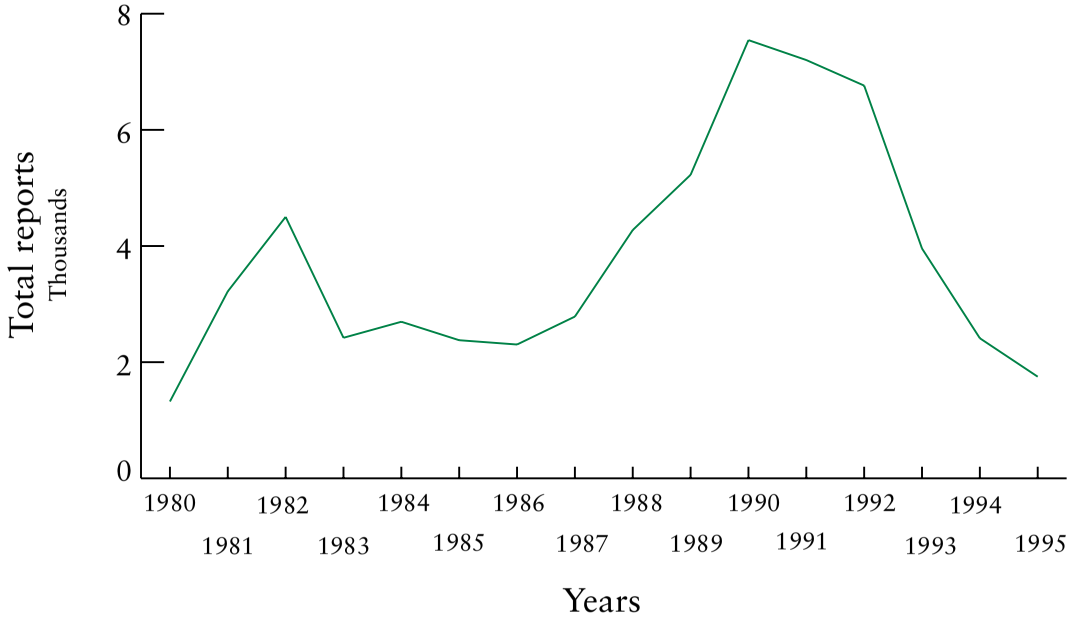
17.2.1 Hepatitis A vaccine is a formaldehyde-inactivated vaccine prepared from either the GBM or the HM 175 strain of hepatitis A virus (HAV) grown in human diploid cells. It is supplied as a suspension in pre-filled syringes.

17.2.2 The vaccine should be stored at 2-8°C but not frozen, and should be protected from light. It should not be diluted or mixed with other vaccines in the same syringe.

17.2.3 Immunogenicity studies show that levels of antibody produced after a primary course of vaccine administered intramuscularly

Laboratory reports of Hepatitis A infection

England and Wales (1980-1995)



Source: PHLS, CDSC

are well in excess of those found after the administration of HNIG. The primary course produces anti-HAV antibodies which persist for at least one year and antibody persistence can be prolonged by administration of a booster dose of vaccine 6 to 12 months after the initial course.

■ 17.2.4 Human normal immunoglobulin may be administered at the same time as vaccine if protection is required less than 10 days after the first dose of hepatitis A vaccine.

■ 17.3 Recommendations

■ 17.3.1 Travellers

Protection against hepatitis A is recommended for travellers to areas of moderate or high HAV endemicity particularly if sanitation and food hygiene are likely to be poor. Active immunisation with hepatitis A vaccine is the preferred method of protection particularly for frequent travellers to such areas or for stays longer than three months. Immunisation is **not** considered necessary for those travelling to Northern or Western Europe (including Spain, Portugal and Italy), or to North America, Australia or New Zealand.

When practicable, testing for antibodies to hepatitis A virus prior to immunisation may be worthwhile in those aged fifty years or over, those born in areas of high or moderate hepatitis A endemicity and those who have a history of jaundice.

Similar considerations will apply to military and diplomatic personnel being posted or likely to be posted to hepatitis A virus endemic countries.

■ 17.3.2 Patients with chronic liver disease

Although patients with chronic liver disease are at no greater risk of acquiring hepatitis A infection, it can produce a much more serious illness in these patients who should therefore be considered for immunisation with hepatitis A vaccine. This will include intravenous drug misusers with chronic liver disease.

17.3.3 Haemophiliacs

Transmission of hepatitis A has been associated with the use of Factor VIII and Factor IX concentrates where viral inactivation procedures do not destroy hepatitis A and it is especially important that haemophiliacs receiving such products should be immunised against hepatitis A. Because of the high incidence of previous infections with hepatitis B and hepatitis C and of pre-existing liver disease in haemophiliacs, infection with hepatitis A can be particularly severe and these haemophiliacs should also be immunised against hepatitis A. Those who are immunosuppressed may respond less well to vaccine, and post-immunisation testing for antibody should be considered.

Haemophiliacs should be immunised subcutaneously.

Haemophiliacs and patients with chronic liver disease should be checked for previous exposure before immunisation

17.3.4 Occupational exposure

Immunisation is recommended for laboratory workers who are working directly with the virus.

There is no evidence that most health care workers are at increased risk of hepatitis A and routine immunisation is not indicated.

Outbreaks of hepatitis A have been associated with residential institutions for the mentally handicapped. Transmission does occur more readily in such institutions and immunisation of staff and residents may be appropriate in the light of local risk assessment. Similar considerations apply in other institutions where standards of personal hygiene are poor.

Infection in young children is likely to be sub-clinical and those working in day care centres and other settings with children who are not yet toilet-trained may be at increased risk of infection. Under normal circumstances, the risk of transmission to staff and children can be minimised by careful attention to personal hygiene but, for example, in the case of local community outbreaks the need for immunisation of staff and children should be discussed with the local Consultant in Communicable Disease Control or in Scotland the CPHM (CD & EH).

There is currently not enough evidence to suggest that immunisation of all sanitation workers against hepatitis A is justified and further epidemiological studies are needed to establish the risks in particular groups of workers. However raw untreated sewage is frequently contaminated with hepatitis A and a potential occupational risk exists in those workers who come into direct contact with untreated sewage. The Control of Substances Hazardous to Health (COSSH) Regulations 1994 require employers to undertake their own risk assessments and to bring into effect measures necessary to protect workers and others who may be exposed, so far as is reasonably practicable, against those risks. For those at risk of exposure to untreated sewage, immunisation against hepatitis A may be indicated as part of those measures.

Food packagers or food handlers in the United Kingdom have not been associated with HAV transmission sufficiently often to justify their immunisation as a routine measure.

17.3.5 Homosexuals

Cases of hepatitis A in homosexual males have been reported in the United Kingdom. Immunisation should be offered to those whose sexual behaviour is likely to put them at risk.

17.3.6 Outbreaks

There is evidence that the use of hepatitis A vaccine can interrupt ongoing community outbreaks of hepatitis A when given to a defined population. Further guidance on the management of outbreaks should be sought from the Consultant in Communicable Disease Control or from the PHLS Communicable Disease Surveillance Centre. In Scotland this should be from the CPHM (CD & EH) or from the Scottish Centre for Infection and Environmental Health. For post exposure prophylaxis for contacts of cases see section 17.9.

17.4 Route of administration and dosage

17.4.1 The immunisation regimen for adults consists of a single dose of vaccine. Antibodies produced in response to this persist for at least one year. A booster dose at 6-12 months after the initial dose results in more persistent antibodies and a substantial increase in antibody titre and will give immunity for up to 10 years.

■ 17.4.2 The immunisation regimen for children and adolescents up to 15 years consists of a single dose of vaccine (720 ELISA units of the HM 175 strain) administered intramuscularly and produces antibodies for at least a year. In order to obtain more persistent immunity for up to 10 years a booster dose (720 ELISA units) is recommended between six and twelve months after the primary course.

The former regimen for children and adolescents up to 15 years consisted of two doses of vaccine (360 ELISA units) administered intramuscularly two weeks to one month apart with a booster dose (360 ELISA units) recommended between six to twelve months after the primary course for prolonged immunity. Where initiated, the manufacturer recommends this regimen should be completed at this dosage.

The vaccine should be given intramuscularly in the deltoid region. It should not be given into the gluteal region because vaccine efficacy may be reduced; nor should it be administered intravenously, or intradermally and should not be routinely given subcutaneously, although the subcutaneous route should be used in haemophiliacs.

■ 17.4.3 **Dosage**

The dose in adults (16 years and over) is 1440 ELISA units (1ml) of the HM 175 strain or 160 Antigen units (0.5ml) of the GBM strain.

The dose in children/adolescents (1-15 years), in a separate presentation, is 720 ELISA units (0.5ml) of the HM175 strain. This will replace the earlier formulation where the dose was 360 ELISA units (0.5ml) (see 17.4.2).

■ 17.5 Adverse reactions

Adverse reactions are usually mild and confined to the first few days after immunisation. The most common reactions are mild transient soreness, erythema and induration at the injection site. General symptoms such as fever, malaise, fatigue, headache, nausea and loss of appetite are also reported less frequently.

It is important that all serious adverse reactions should be reported to the Committee on Safety of Medicines by the yellow card system.

17.6 Contraindications

Immunisation should be postponed in individuals suffering from severe febrile illness.

The effect of HAV vaccine on fetal development has not been assessed. Since it is an inactivated vaccine, the risks to the fetus are likely to be negligible but, as with other vaccines in pregnancy, it should not be given unless there is a definite risk of infection.

17.7 Supplies of Hepatitis A Vaccine

Pasteur Merieux MSD Ltd, Tel. 01628 773200
Avaxim (adults) GBM strain

SmithKline Beecham, Tel. 0181-913 4290
Havrix Monodose (adults)
Havrix Monodose Junior (children and adolescents up to 15 years)
Havrix Junior (children and adolescents up to 15 years)
Havrix (all preparations) HM175 strain

17.8 Immunoglobulin

17.8.1 Human normal immunoglobulin (HNIG) offers short-term protection (up to about four months) against infection with hepatitis A to those in close contact with cases and to those travelling to areas where infection is more prevalent, particularly if sanitation and food hygiene are likely to be poor.

17.8.2 Although infection is commonly subclinical in young children and severe infection uncommon, the decision to use HNIG may be influenced by the wish to protect parents and other adult contacts. Evidence suggests that, even if HNIG modifies disease rather than preventing infection, it is effective in preventing secondary cases.

17.8.3 There is no evidence associating the administration of intramuscular immunoglobulin with transmission of HIV. Not only does the processing of the plasma from which it is prepared render it safe, but the plasma is derived from blood from donors screened for HIV, hepatitis B and hepatitis C.

17.9 Recommendations

Use of HNIG should be considered in the following circumstances:

a Contacts of cases of hepatitis A infection

Prophylaxis restricted to household and close contacts may be relatively ineffective in controlling further spread. If given to a wider social group of recent household visitors (kissing contacts and those who have eaten food prepared by the index case) spread may be more effectively prevented.

b Outbreaks

The appropriate approach to prophylaxis and the use of HNIG, with or without hepatitis A vaccine, should be discussed with the Consultant in Communicable Disease Control or CPHM (CD & EH) in Scotland.

In schools, particularly nursery and primary schools, HNIG may be used to protect teachers, adult helpers, including those responsible for cleaning the toilets, and the children and parents of children in the affected classes.

In closed communities where personal hygiene may be poor, widespread use of HNIG should be considered.

c Travellers

HNIG is an alternative to vaccine for those travelling occasionally and for short periods to countries outside Northern and Western Europe, North America, Australia and New Zealand. Hepatitis A vaccine is preferable for those visiting such countries frequently or staying for longer than three months (see 17.3.1).

Where practicable, testing for antibodies to hepatitis A virus prior to immunisation may be worthwhile in those aged fifty years or over, those born in areas of high or moderate endemicity and those who have a history of jaundice.

HNIG may interfere with the development of active immunity from live virus vaccines. It is therefore wise to administer live virus vaccines at least three weeks before the administration of immunoglobulin. If immunoglobulin has been administered first, then an interval of three months should be observed before administering a live virus vaccine.

This does not apply to yellow fever vaccine since HNIG does not contain antibody to this virus. For travellers, if there is insufficient time, the recommended intervals may have to be ignored, especially where polio vaccine is concerned. Alternatively, hepatitis A vaccine may be used in these circumstances.

17.10 Dosage

At present, the dosage of HNIG is expressed either by weight (mg) or by volume (ml). 1ml of a 16% solution contains 160 mg. There are two dosage levels. The higher dose is recommended for those at greater risk (ie contacts) and for extended protection (ie those travelling abroad for 3-5 months).

Age	Low dose For travel lasting 2 months or less	High dose For travel lasting 3-5 months and for contacts
Under 10years	125 mg	250 mg
10years and over	250 mg	500 mg
or		
All ages	0.02-0.04 ml/kg	0.06-0.12 ml/kg

17.11 Supplies

Bio-Products Laboratory Tel. 0181 905 1818
Scottish National Blood Transfusion Service Tel. 0131 664 2317
Northern Ireland Public Health Laboratory, Belfast City Hospital Tel. 01232 329241

Immuno (Gammabulin), Tel. 01732 458101

Kabi Pharmacia (Kabiglobulin), Tel. 01908 661101

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For contacts and the control of outbreaks only:

PHLS Communicable Disease Surveillance Centre,
Public Health Laboratories, England and Wales Tel. 0181 200 6868

Scottish Centre for Infection and Environmental Health, Glasgow (Tel. 0141 9467120).