

CLINICAL UPDATE

A Vaccine Preventable Disease

Hepatitis A

2nd Edition 2007

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Digestive Health Foundation

The Digestive Health Foundation (DHF) is an educational body committed to promoting better health for all Australians by promoting education and community health programs related to the digestive system.

The DHF is the educational arm of the Gastroenterological Society of Australia, the professional body representing the specialty of gastrointestinal and liver disease in Australia. Members of the Society are drawn from physicians, surgeons, scientists and other medical specialties with an interest in GI disorders.

Since its establishment in 1990 the DHF has been involved in the development of programs to improve community awareness and the understanding of digestive diseases.

Research and education into gastrointestinal disease are essential to contain the effects of these disorders on all Australians.

Guidelines for General Practitioners and patient leaflets are available on a range of topics related to GI disorders. Copies are available by contacting the Secretariat at the address below.

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DEFINITION

The hepatitis A virus (HAV) causes infection of the liver and is a major cause of illness worldwide.

HAV is a small RNA virus, a member of the Hepatovirus genus of the picornavirus family, which can survive in food and water and is relatively resistant to detergents. The virus was first identified in human faeces in 1973 and later identified in blood. HAV is primarily a human infection but has been also identified in nonhuman primates. Hepatitis A causes acute hepatitis only and does not lead to chronic liver disease.

Hepatitis A is a vaccine preventable disease.

EPIDEMIOLOGY

Hepatitis A virus replicates in hepatocytes and is secreted via bile into the intestine. Faeces contains large amounts of virus, thus the primary mode of transmission is faecal-oral in contrast to the parenteral or blood-borne spread of hepatitis B and C.

In Australia, most transmission of hepatitis A is from person to person, often among family members in the same household, between sexual partners (especially from oral-anal contact) and among people who have occupational exposure to the virus, such as child-care centre workers or those employed in residential institutions.

Large community-wide outbreaks have occurred, related to gatherings or groups of people who transmit infection among themselves, and potentially to the broader community. Food and water may be contaminated with virally-infected faeces resulting in epidemics of acute hepatitis A, although this is uncommon in Australia. In the USA and Australia, pollution of shellfish breeding sites has led to outbreaks of hepatitis A from ingestion of raw oysters. For a short period of time, hepatitis A virus is also present in serum and it is thought that blood to blood transmission can occur. Outbreaks of hepatitis A have been reported amongst injecting drug users in Australia, although it is unclear whether transmission is faecal-oral or blood-borne in this setting. Exposure to saliva or urine

from an infected person is unlikely to transmit the virus. Intrauterine transmission has not been reported. As many as 40% of patients have no identifiable risk factor.

The prevalence of hepatitis A infection worldwide is variable. Reported figures are probably an underestimate since many cases are subclinical. In developing countries with poor hygiene and sanitation, infection with hepatitis A peaks at an early age, usually under 5 years, so that the majority of the population will develop immunity. Such areas include parts of Africa, Asia, Central and South America. In areas of intermediate endemicity such as Eastern Europe and Russia the infection appears to peak in older childhood and adolescence. Finally in low prevalence areas such as North America, Western Europe and Australia, hepatitis A is largely seen in certain at-risk groups. These include travellers to areas of high prevalence, injecting drug users, and men who have sex with men. In Australia there has been a higher prevalence of hepatitis A infection in Aboriginal communities.

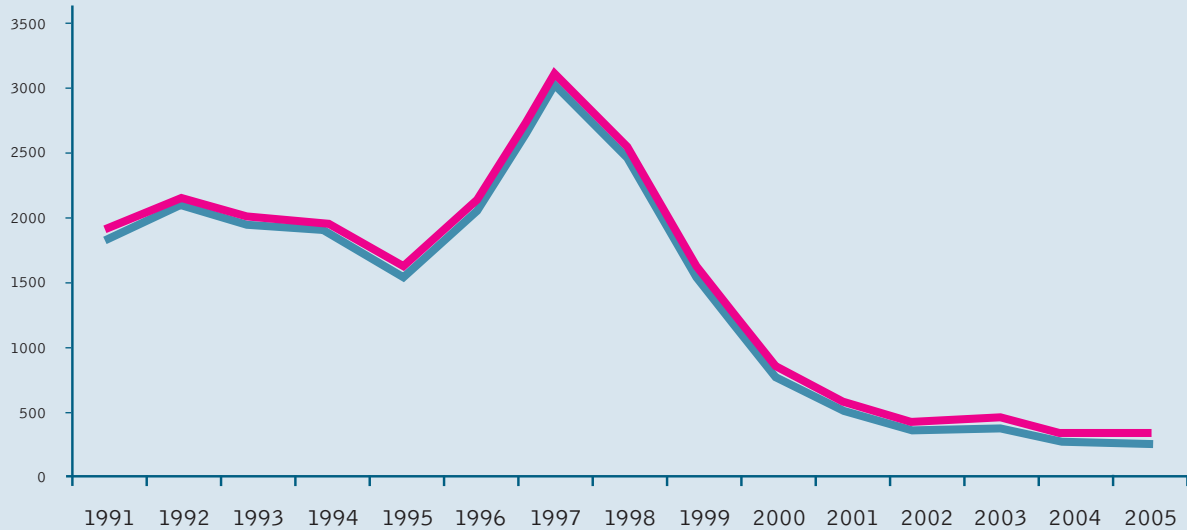
In most areas of Australia where sanitation and hygiene are well-developed, fewer than 30% of people have been exposed to the hepatitis A virus. However outbreaks of hepatitis A still occur with household and community spread. Hepatitis A notifications in Australia have reduced markedly since the introduction of vaccination to high risk groups in the late 1990s.

CLINICAL FEATURES

The incubation period (time between exposure to the virus and the development of signs and symptoms) varies between 15 and 40 days and averages 28 days. Viral shedding in faeces reaches a peak just before clinical symptoms become apparent and thus patients are most infectious prior to the onset of symptoms.

Faeces are usually no longer infectious by two weeks after jaundice becomes apparent. The onset of symptoms are anorexia, nausea, vomiting, abdominal pain and mild fever. Less frequent symptoms include diarrhoea, myalgias, pruritis and headache. Common signs are jaundice, hepatomegaly, dark urine

Hepatitis A notifications in Australia 1991 to 2005.



Source: National Notifiable Diseases Surveillance System 2006

and pale-coloured faeces. Jaundice lasts from 1 to 10 weeks (average 6 weeks). Atypical manifestations include relapse in around 10% (suggested by a second peak in serum aminotransferases) and prolonged cholestasis in about 5%.

Age is an important determinant of clinical severity. Only 5% of children under 4 years of age and less than 10% of children aged 6 years develop jaundice. Thus infants and young children may appear quite well or have only mild non-specific symptoms. Children over the age of six and adults will develop jaundice in 75% of cases and will come to the attention of their local doctor and communicable diseases surveillance authorities.

Most patients will recover completely by two or three months after the onset of symptoms and the remainder by six months. Rarely, acute hepatitis A may progress to fulminant hepatic failure with development of coagulopathy and encephalopathy, and death occurs in 0.2% of cases. The likelihood of severe disease and death is much greater in patients 50 years of age or older and in those patients with chronic liver disease due to hepatitis B or alcohol. However, HAV infection itself never causes chronic liver disease.

Laboratory diagnosis

Liver function test abnormalities in acute hepatitis A infection include increased serum bilirubin and serum aminotransferase (ALT and AST) values which may be elevated 10 - 100 fold over the reference range. An important indicator of severe liver disease is coagulopathy as measured by the INR.

Acute hepatitis A infection is confirmed by the detection of IgM antibodies to HAV, which are present in high titre and provide a specific serological diagnosis early in the course of the disease. As the host immune response eradicates the virus, specific IgG antibodies appear and the IgM response wanes. Persistent neutralising IgG antibodies against HAV provide lifelong immunity to further infection from hepatitis A but not other hepatitis viruses.

Treatment

The treatment of acute HAV infection is supportive with adequate rest and attention to fluid intake. Medications should be limited to those considered essential; sedatives and narcotics should be avoided in acute hepatitis, as should alcohol.

Hospitalisation may be required for patients unable to maintain adequate fluid intake because of nausea or vomiting. It is prudent to follow serial liver function tests, including clotting studies, until a peak has been reached and a trend towards normalisation is evident. The development of liver failure may be associated with a prolonged INR despite rapidly falling serum transaminases or the development of hepatic encephalopathy or ascites.

Prevention

General measures Avoiding exposure to the virus by paying attention to personal hygiene such as hand washing prior to eating or drinking is a simple measure. Sanitation procedures aimed at safe water supply and sewage disposal have led to a significant decrease in transmission of this virus. The community should be aware of the large outbreaks which have occurred after eating raw shellfish.

Immunisation

Passive immunisation The administration of normal human immunoglobulin (NHIG) has been used for many years to passively immunise persons either after exposure to a family member or close contact with acute hepatitis A or before travel to an endemic area. NHIG is given to close contacts who have had contact with a case during the 2 weeks before, or up to one week after, the onset of jaundice. It is given at doses of 0.5 mL to 2.0 mL according to body weight and is 90% effective in preventing clinical hepatitis with protection lasting about 3 months. The use of NHIG in travellers to high risk areas has been largely replaced by hepatitis A vaccination, although should still be considered when departure is imminent, and in infants. NHIG is inexpensive and effective, but limited in availability.

Active immunisation In the 1990s, formalin-inactivated hepatitis A vaccines were developed and approved for use after several large efficacy trials demonstrated high rates of protection. As of 2006, five monovalent hepatitis A vaccines, 2 combined hepatitis A/hepatitis B vaccines and a combined hepatitis A/typhoid vaccine are available in Australia. All are administered by the intramuscular route. Vaccine dose and schedules vary according to age, and can be obtained from the Australian Immunisation Handbook or specific Product Information documents.

By 4 weeks after vaccination with any of these vaccines, more than 90% of adults will seroconvert with high anti-HAV titres. In children, almost 100% will seroconvert by 4 weeks. The vaccines have a very high protective efficacy of 98-100%, and are protective throughout the world, as only a single hepatitis A serotype exists. With the combination HAV/HBV vaccines, virtually all recipients develop immune to HAV and more than 90% develop immunity to HBV after the first 2 doses of a 3 dose regimen.

Should doctors screen for HAV IgG to detect individuals who are immune from previous natural HAV infection? In countries with a low prevalence of HAV such as Australia, screening may only be cost-effective for patients born before 1950, those who spent their early childhood in endemic areas and those with an unexplained previous episode of hepatitis or jaundice. If a person is found to have total (or IgG) anti-HAV, then previous infection or vaccination can be assumed, and hepatitis A vaccination is not required.

Immunisation of Indigenous Children

Vaccination of Indigenous children was introduced in north Queensland in February 1999 and led to virtual eradication of hepatitis A from Indigenous communities. In addition, there was a marked reduction in infection in non-Indigenous people. This finding supports the concept that targeting of a high risk population within a community can significantly reduce disease in the broader community.

From November 2005, the Australian government has provided free hepatitis A vaccine for all Indigenous children aged five years and under living in Queensland, the Northern Territory, Western Australia and South Australia. The vaccine is administered in two doses, with the first dose after 12 months of age, and the second dose six months later.

Hepatitis A Vaccines

Avaxim (Aventis Pasteur)

Havrix Junior (GlaxoSmithKline)

Havrix 1440 (GlaxoSmithKline)

VAQTA Paediatric Adolescent Formulation (CSL Vaccines/Merck Sharp & Dohme)

VAQTA Adult Formulation (CSL Vaccines/Merck Sharp & Dohme)

Combined Hepatitis A/Hepatitis B Vaccines

Twinrix Junior (360/10) (GlaxoSmithKline)

Twinrix (720/20) (GlaxoSmithKline)

Combined Hepatitis A/Typhoid Vaccine

Vivaxim (Aventis Pasteur)

WHO SHOULD RECEIVE HEPATITIS A VACCINE?

Potential vaccine recipients including those recommended by the National Health and Medical Research Council include:

- Travellers from areas of low endemicity to moderate or high endemicity, including military personnel, business travellers, backpackers, expatriates, diplomats, aid workers, missionaries
- Men who have sex with men
- Injecting drug users
- Recipients of blood and blood products (such as those used for treatment of inherited clotting disorders)
- The intellectually disabled and their carers
- Persons with occupational exposure to the virus:
 - Child day-care centre, preschool or residential institutional workers
 - Laboratory workers exposed to biological specimens
 - Foodhandlers
 - Nursing staff and other healthcare workers in contact with patients in paediatric wards, infectious diseases wards, emergency rooms and intensive care units

- Sewage treatment workers
- Those working in rural and remote Indigenous communities
- Patients with chronic liver disease (chronic HBV, HCV, alcoholic cirrhosis, etc).

The National Health and Medicine Research Council recommends consideration of combined hepatitis A/hepatitis B vaccines for those at risk of both infections. These include:

- Expatriates and long-term visitors to developing countries
- Medical, dental and nursing undergraduate students
- Men who have sex with men
- Injecting drug users
- Patients with chronic liver disease
- The intellectually disabled and their carers
- People with haemophilia who may receive pooled plasma concentrates

See references in "Further reading" section.

FURTHER READING

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ACKNOWLEDGEMENTS

This second edition has been prepared by the Digestive Health Foundation, of the Gastroenterological Society of Australia. Every care has been taken in its compilation. The booklet is intended to be used as a guide only and not as an authoritative statement of every conceivable step or circumstance which may or could relate to the management of hepatitis A.

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Information leaflets on hepatitis A for patients and the general public are available through the Digestive Health Foundation, 145 Macquarie Street, Sydney, NSW, 2000.
www.gesa.org.au





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