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Hepatitis A

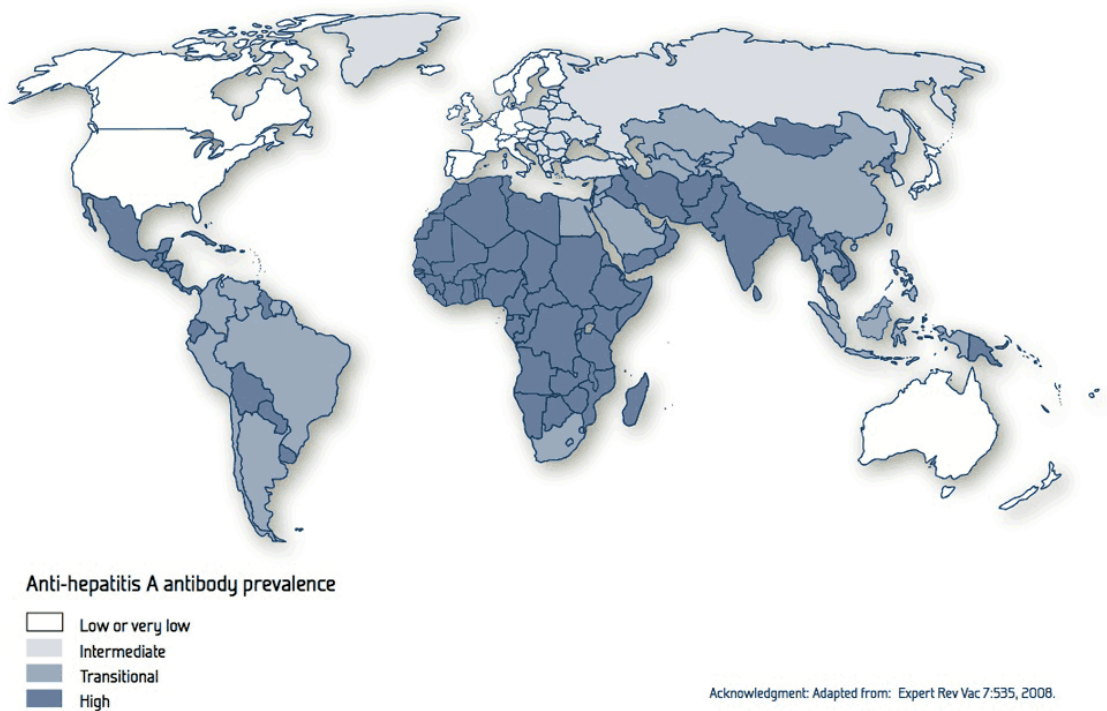
Introduction

Hepatitis A is a small, unenveloped RNA virus within the genus *Hepatovirus*, a member of the Picornavirus family. It causes acute inflammation of the liver.

Epidemiology

Global Epidemiology

Figure 1: Hepatitis A antibody prevalence



Map from: Health Information for Overseas Travel, 2010 [1]

The incidence of hepatitis A is closely related to socio-economic conditions, and sero-epidemiological studies show that prevalence of anti-hepatitis A antibodies varies from 15% to close to 100% in different parts of the world [2]. An estimated 1.5 million clinical cases of hepatitis A occur worldwide each year. The disease is endemic in many low-income countries where food and water hygiene may be of a low standard.

Regions where hepatitis A is highly endemic include the Indian sub-continent (particularly India, Pakistan, Bangladesh and Nepal), Sub-Saharan and North Africa, parts of the Far East (except Japan), South and Central America and the Middle East. Clinical cases of hepatitis A in adults are



uncommon in highly endemic countries, as most people have been exposed to the virus at a young age and have acquired life-long immunity. Most high-income countries such as those in Western and Northern Europe, North America, Australia, New Zealand and Japan are of low endemicity for hepatitis A. The majority of the population in these countries will have no immunity to hepatitis A and are therefore susceptible to the infection.

In some countries of the Middle East, the Americas and Asia there has been a reduction in endemicity [3]. These countries are now in transition from high to intermediate and low endemicity, such that hepatitis A is more common in young adults and teenagers who may not have had previous exposure to the virus as a child (and therefore not acquired any immunity) [2].

Hepatitis A is now relatively unusual in the UK and is more often associated with specific risk groups (such as injecting drug users) or travel to an endemic country [4]. Since the mid-1990s there has been a decline in laboratory-confirmed cases of hepatitis A reported in England and Wales [4, 5]. However, travel history or other risk factor information is seldom reported, so it is difficult to say whether the decline is due to a change in travel patterns or to other factors.

Between 2005 and 2009 there were 84 reported cases of hepatitis A with a known recent history of foreign travel (4% of the total) [4]. The area of travel was known for 75 of these cases. The majority of cases were associated with travel to: Pakistan (21), Egypt (11), and India (9).

Risk for travellers

The risk of acquiring hepatitis A in high-income countries is low. Non-immune travellers are at risk of contracting the disease during visits to countries of high or intermediate endemicity. The risk during travel depends on living conditions, length of stay and standards of food and water hygiene. Those at higher risk include travellers visiting friends and relatives (VFRs) [6], long-term travellers, and those visiting areas of poor sanitation. However, cases have occurred in tourists staying in good quality hotel accommodation [7].

Hepatitis A remains one of the most common travel-related vaccine preventable diseases. However, the incidence in travellers is declining. A study published in 2006 found the incidence of hepatitis A amongst non-immune travellers varied between six and 30 cases per 100,000 travellers per month [8]. The highest rates were in travellers to Africa, south-central Asia, particularly the Indian sub-continent and Latin America. A study in 2009 found that the highest incidence rates in Swedish travellers were in those to East Africa followed by the Middle East and the Indian sub-continent [9].

Transmission

Hepatitis A is usually acquired through food or water contaminated by human faeces; foods that grow close to the ground such as strawberries and lettuce can be a risk. Crustaceans that feed at the bottom of the ocean such as oysters and clams can concentrate the virus and be a risk if ingested under-cooked or raw. Food handlers excreting hepatitis A virus can contaminate foods if they do not observe proper hygiene.



Person to person transmission in conditions of poor faecal hygiene is also a risk factor. This mode of transmission can occur during certain sexual practices (e.g. oral/anal sexual contact), through unhygienic injection drug use, and between children [10].

Virus shedding in the faeces occurs during the incubation period of hepatitis A, and continues for a few days after the onset of jaundice. It is at this stage that patients are most infectious. Virus shedding can be prolonged in immunocompromised persons.

Signs & symptoms

Hepatitis A is usually a sub-clinical illness in young children. However, the disease becomes more serious with advancing age, with approximately 2% mortality rate in those over 50 years of age [11].

After an average incubation period of 28 days (range of 15-50 days), patients can experience a prodrome of malaise, anorexia, nausea and fever before developing jaundice [2]. Recovery takes about a month in young people, but some patients are ill for many weeks. Complications are more likely in those with pre-existing chronic liver disease, and include fulminant hepatitis.

Following infection with hepatitis A, patients acquire life long immunity.

Treatment

There is no specific anti-viral treatment for hepatitis A, but rather supportive intervention.

Prevention

Hepatitis A is transmitted via the faecal-oral route; therefore the most common mode of infection for travellers is through eating contaminated food, or drinking contaminated water. The risk of acquiring hepatitis A can be reduced by following guidelines on [food and water hygiene](#) and by ensuring good personal hygiene.

Several effective and well-tolerated hepatitis A vaccines are available for travellers intending to visit endemic areas. The vaccine is a complement to food and water hygiene precautions.

Hepatitis A Vaccine Information

Indications for use of vaccine

Hepatitis A vaccine is recommended for:

- Travellers visiting areas of hepatitis A risk, particularly those visiting friends and relatives, long-term travellers and those visiting areas of poor sanitation;
- Persons with chronic liver disease. Although not at greater risk of hepatitis A infection, the disease can produce a more serious illness in this group;
- Persons whose sexual behaviour is likely to put them at an increased risk. There is an increase in hepatitis A in men who have sex with men [10];
- Vaccination should be given to injecting drug users and those with chronic liver disease, haemophilia, or at occupational risk.



Further information on indications for vaccination can be found in [Immunisation against Infectious Disease known as the 'Green Book'](#).

Country-specific information on the risk of hepatitis A can be found in the [NaTHNaC Country Information Pages](#).

Availability of vaccine

Several vaccines are licensed for use in the UK, all of which are inactivated.

Details of these can be found in the summary table below.

Combined hepatitis A and B vaccines, and combined hepatitis A and typhoid vaccines are also available.

Vaccine schedules (listed alphabetically) [12-21]

Vaccine	Manufacturer/distributor	Schedule	Length of protection against hepatitis A*	Age range
Ambirix Combined hepatitis A and B	GlaxoSmithKline	2 doses, given 6-12 months apart	Hepatitis A: 10 years following 2 nd dose. See also hepatitis B information sheet	Children from 1 to 15 years
Avaxim	Sanofi Pasteur MSD	2 doses, given 6-12 months apart	10 years following 2 nd dose	Adults from 16 years
Epaxal	Crucell UK Ltd	2 doses, given 6-12 months apart	Up to 30 years following 2 nd dose	Adults & children from 1 year
Havrix Monodose	GlaxoSmithKline	2 doses, given 6-12 months apart	Up to 25 years following 2 nd dose	Adults from 16 years
Havrix Junior Monodose	GlaxoSmithKline	2 doses, given 6-12 months apart	Up to 25 years following 2 nd dose	Children from 1 to 15 years
Hepatyrix	GlaxoSmithKline	1 dose	Up to 25	Adults and

Combined hepatitis A and typhoid		followed by a single antigen hepatitis A vaccine 6-12 months later	years following 2 nd dose. See also typhoid information sheet	children from 16 years
Twinrix Adult Combined hepatitis A and B	GlaxoSmithKline	3 doses, 0, 1, and 6 months	Hepatitis A: up to 25 years following 3 rd dose. See also hepatitis B information sheet	Adults and children from 16 years
		4 doses, days 0, 7 and 21, 4 th dose at 12 months.	Hepatitis A: up to 25 years following 4 th dose. See also hepatitis B information sheet	Adults aged 18 years above
Twinrix Paediatric Combined hepatitis A and B	GlaxoSmithKline	3 doses, 0, 1 and 6 months	Hepatitis A: up to 25 years following 3 rd dose. See also hepatitis B information sheet	Children from 1 to 15 years
Vaqta Paediatric	Sanofi Pasteur MSD	2 doses, given 6-18 months apart	At least 9 years following 2 nd dose	Children from 2 to 15 years
ViaTIM Combined hepatitis A and typhoid	Sanofi Pasteur MSD	1 dose followed by a single antigen hepatitis A vaccine 6-12 months later	10 years following 2 nd dose. See also typhoid information sheet	Adults and children from 16 years



* There is no evidence that further reinforcing doses of hepatitis A vaccine are needed in immunocompetent individuals following completion of the primary course [22]. The duration of protection from a completed course of vaccine can be expected to be at least 20 years and probably indefinite. The Joint Committee on Vaccination and Immunisation (JCVI) has accepted a 20 year interval for a booster dose of vaccine for those at ongoing risk. However, specific advice should be sought for individuals with altered immune responses.

It is good practice to continue a course of hepatitis A with the same brand of vaccine. However, evidence suggests that hepatitis A vaccines are likely to be compatible with each other [22-24], and if necessary a different preparation of hepatitis A vaccine could be given.

Interrupted courses

The Summary of Product Characteristics (SPC) for Avaxim states that the second dose may be administered up to 36 months after the primary dose [12].

The SPC for Epaxal states that the second dose can be delayed for up to 10 years [14].

The SPC for Havrix Monodose states that a second dose that is delayed for up to 5 years can be expected to induce similar antibody levels as a booster given within the recommended 6-12 months [15]. For Havrix Junior Monodose, a booster that is delayed for up to 3 years can be expected to induce similar antibodies as a second dose given within the recommended 6-12 months [16].

Vaqta Paediatric second doses can be administered up to 18 months following the primary dose [20].

Although booster doses delayed beyond the recommended intervals described above are not covered by the product licence, research indicates that a second dose given at long intervals will still result in a boosting immune response [24-28].

Thus, based on evidence from available studies, there is no maximum interval which would require restarting a course of hepatitis A vaccine.

Contraindication

- Current febrile illness
- Individuals who develop hypersensitivity reactions after vaccination should not receive further doses

Specifically relating to Epaxal

- Hypersensitivity to eggs and chicken protein

Adverse events

Adverse reactions following hepatitis A vaccine tend to be mild and transient. They include tenderness, redness and swelling at the injection site. Less commonly, fever, headaches, dizziness and malaise have been reported.



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Links

- [Health Protection Agency Hepatitis A](#)
- [Immunisation against infectious disease 'The Green Book'](#)
- [NaTHNaC Health Information Sheet on Prevention of food- and water-borne diseases](#)