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## Hepatitis A

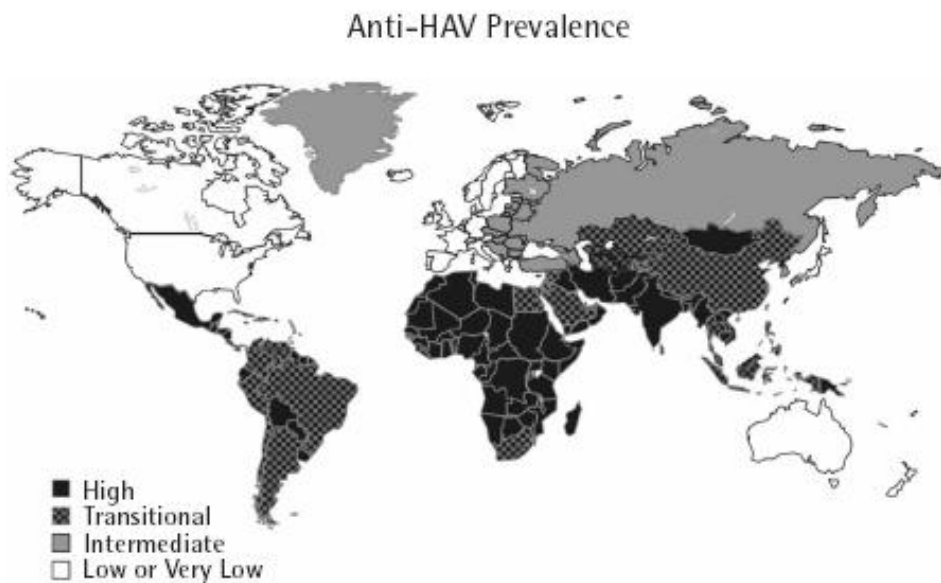
### Introduction

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: Geographic distribution of the prevalence of hepatitis A virus [1].



Hepatitis A occurs worldwide; it is estimated that around 1.5 million cases of clinical hepatitis A occur per year [2]. 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]. 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, and parts of the Far East (not Japan), South and Central America, and the Middle East (Figure 1). 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, and 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 as children and adults.

In some countries in parts of Asia and the Americas there has been a reduction in endemicity. 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 (and therefore not acquired any immunity) to the virus as a child [1].

### Hepatitis A in travellers from England, Wales, and Northern Ireland

Figure 2: Laboratory reports of hepatitis A, England, Wales, and Northern Ireland: 1998-2007

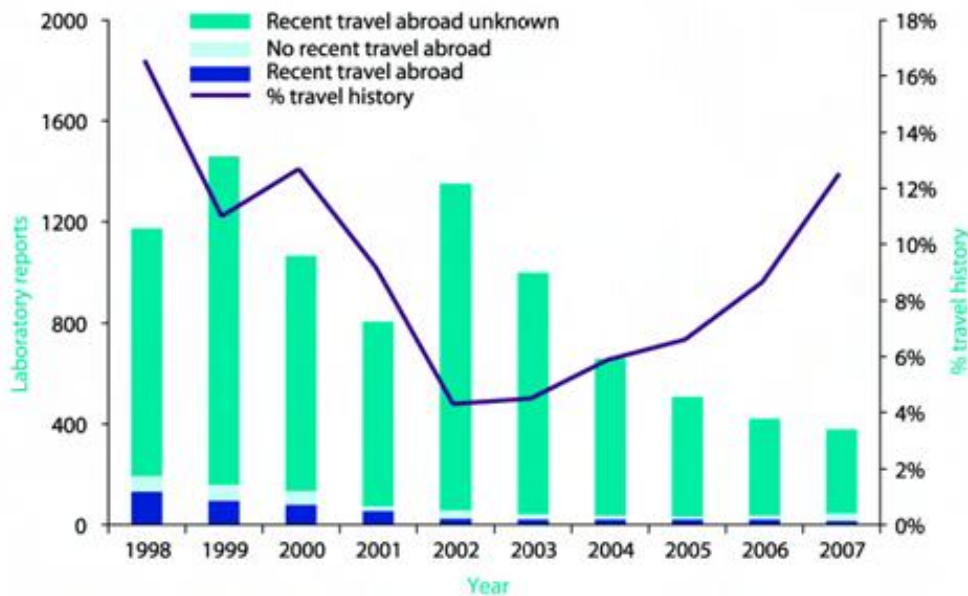


Figure 2 shows the laboratory reports of hepatitis A to the Health Protection Agency, Centre for Infections between 1998 and 2007 [3]. There has been a decline in reported hepatitis A cases seen (in total) in England, Wales, and Northern Ireland since the mid-1990s. The majority of laboratory reports do not have a travel history so it is not possible to say where most of the cases were acquired.

In 2006 and 2007 there were 36 reported cases of hepatitis A with a recent history of foreign travel. Of those, 21 (58%) had travelled to the Indian subcontinent (17 to Pakistan, 3 to Bangladesh, 1 to India).

**Table 1. Countries of travel for travel-associated cases of hepatitis A in 2006 and 2007**

Country of travel	Laboratory reports of hepatitis A
Pakistan	17
Egypt	5
Thailand	3
Bangladesh	3
India	1
Nigeria	1
Philippines	1
Singapore	1
Spain	1
Sudan	1
Turkey	1
Uzbekistan	1
<b>Total</b>	<b>36</b>

### 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 depends on several factors including living conditions, length of stay and standards of food and water hygiene. Those at higher risk include travellers visiting friends and relatives, long-term travellers, and those visiting areas of poor sanitation. However, cases have occurred in tourists staying in good quality hotel accommodation.

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 [4]. The highest rates were in travellers to Africa, south-central Asia, particularly the Indian sub-continent, and Latin America.

### Transmission

Hepatitis A in travellers is usually acquired through food or water contaminated by human faeces. As examples, foods that grow close to the ground such as strawberries and lettuce may 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 between children, or in adults during certain sexual practices and when using injection drugs [5].

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 [6].

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 common sense guidelines on [food and water hygiene](#) and by ensuring good personal hygiene.

Several highly 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. An increase in hepatitis A has been noted in men who have sex with men [5];
- Vaccination should also 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 'the Green Book'](#).

### 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 hepatitis A and typhoid vaccines are also available.

**Vaccine schedules (listed alphabetically) [7-16]**

Vaccine	Manufacturer/distributor	Schedule	Length of Protection*	Age range
Ambirix  Combined hepatitis A and B	GlaxoSmithKline	2 doses, given 6-12 months apart	Hepatitis A: 10 years following 2 <sup>nd</sup> dose* See <a href="#">hepatitis B information sheet</a>	Children from 1 to 15 years
Avaxim	Sanofi Pasteur MSD	2 doses, given 6-12 months apart	10 years following 2 <sup>nd</sup> dose*	Adults from 16 years
Epaxal	Berna Biotech/Masta Ltd	2 doses, given 6-12 months apart	20 years following 2 <sup>nd</sup> dose*	Adults & children from 1 year
Havrix Monodose	GlaxoSmithKline	2 doses, given 6-12 months apart	Up to 25 years following 2 <sup>nd</sup> dose*	Adults from 16 years
Havrix Junior Monodose	GlaxoSmithKline	2 doses, given 6-12 months apart	Up to 25 years following 2 <sup>nd</sup> dose*	Children from 1 to 15 years
Hepatyrix  Combined hepatitis A and typhoid	GlaxoSmithKline	1 dose followed by a single antigen hepatitis A vaccine 6-12 months later	Up to 25 years following 2 <sup>nd</sup> dose* See <a href="#">typhoid information sheet</a>	Adults and 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 <sup>rd</sup> dose*. See <a href="#">hepatitis B information sheet</a>	Adults and children from 16 years
		4 doses, day 0, 7 and 21, 4 <sup>th</sup> dose at 12 months.	Hepatitis A: up to 25 years following 4 <sup>th</sup> dose*. See <a href="#">hepatitis B information sheet</a>	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 <sup>rd</sup> dose*. See <a href="#">hepatitis B information sheet</a>	Children from 1 to 15 years
Vaqta Paediatric	Sanofi Pasteur MSD	2 doses, given 6-18 months apart	At least 9 years following 2 <sup>nd</sup> 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 <sup>nd</sup> dose* See <a href="#">typhoid information sheet</a>	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 [17]. 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 [18,- 20], 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 [8].

The SPC for Epaxal states that the second dose can be delayed for up to 4 years. Good protective antibody levels are achieved even if the booster dose of Epaxal is given up to 56 months after the primary dose [9].

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. 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.

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

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 [19, 21-23].

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



## Contraindications

- 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'](#)