

Hepatitis A vaccines – July 2012

WHO position paper

Summary

The current document replaces the 2000 position paper on hepatitis A vaccines.

Hepatitis A virus (HAV) is transmitted primarily via the faecal/oral route and the incidence of hepatitis A is strongly correlated with access to clean water and adequate sanitation. According to WHO estimates, 212 million cases of acute hepatitis A occurred in 2005.

In low-income regions, exposure to HAV tend to occur before the age of 5 years, when HAV infection is usually asymptomatic. In high-income regions, the risk of acquiring HAV infection is low. In most middle-income regions there is a mix of intermediate and low prevalences and here, a substantial proportion of adolescents and adults are susceptible. HAV infection in these age groups is associated with a higher rate of severe clinical manifestations and hence, transition from high to intermediate endemicity may result in increased incidence of clinically significant disease and mortality from hepatitis A.

Other groups at high risk of HAV exposure and disease include travellers to areas of high endemicity, men who have sex with men, and injection drug users. Groups at risk of serious clinical outcome, once infected, include the elderly and immunocompromised individuals.

The clinical manifestations of acute viral hepatitis typically include non-specific symptoms such as malaise, fatigue, anorexia, vomiting, abdominal discomfort, and diarrhoea. Elevated levels of liver enzymes, the appearance of dark urine and sometimes clay-coloured stools and jaundice are characteristic manifestations. Hepatitis A resolves completely in >99% of the cases. Rare fatalities (0.1% in children <15 years of age and 2.1% in adults \geq 40 years of age) are associated mainly with the development fulminant hepatitis.

Two types of hepatitis A vaccines are currently used worldwide: (a) formaldehyde inactivated vaccines and (b) live attenuated vaccines. Following immunization, a positive test for total anti-HAV antibodies is considered to signify immunity to hepatitis A.

a) Inactivated hepatitis A vaccines, alone or in fixed combinations, are widely used internationally. These vaccines are licensed for use in persons \geq 12 months of age and the manufacturers recommend a 2-dose schedule with 6–12 (up to 18-36) months interval between the 2 doses. Inactivated hepatitis A vaccines are interchangeable and can be administered simultaneously with any other routinely used vaccine.

In general, 2 doses of inactivated hepatitis A vaccine induce protective efficacies of 90-95%, or more. The median predicted duration of protection has been estimated at 45.0 years.

High vaccine efficacy can be achieved also with one single dose of inactivated hepatitis A vaccine: 6 years after implementation of country-wide, annual immunization with a single dose of vaccine to 12-months old children in Argentina, no hepatitis A cases has been detected among vaccinated individuals. Studies among adult travellers confirm that 1 dose of hepatitis A vaccine induces immunological memory and in most cases, anti-HAV antibodies that persist throughout 4–11 year periods of observation.

High efficacy of post-exposure prophylaxis against hepatitis A using one single dose of inactivated vaccine within 2 weeks of exposure is documented.

Cumulative global experience from the use of several hundred million doses of inactivated hepatitis A vaccines testify to their excellent overall safety profile.

b) Live attenuated hepatitis A vaccines are manufactured in China. One dose of this vaccine is used in children aged ≥ 1 year in several national immunization programmes. Controlled trials conducted among large numbers of children 1-15 years of age have shown up to 100% efficacy for pre-exposure prophylaxis and 95% efficacy for post-exposure prophylaxis. Anti-HAV antibodies were detected in 72-88% of the vaccinees 15 years after vaccination. No substantial safety concerns have been identified during these trials. However, live attenuated vaccines are not recommended for use in pregnant women and in immune compromised patients.

Estimates of cost-effectiveness of hepatitis A vaccination in high- and middle income countries show lower ratios for universal vaccination as compared to more targeted vaccination. Universal vaccination was found to be particularly cost-effective in children in high incidence areas.

WHO concludes that both inactivated and live attenuated hepatitis A vaccines are safe and highly immunogenic and that in most cases, these vaccines will generate long-lasting, possibly life-long, protection against hepatitis A both in children and adults.

-Vaccination against HAV should be part of a comprehensive plan for the prevention and control of viral hepatitis. If indicated on the basis of age-specific epidemiological studies and consideration of cost-effectiveness, vaccination against hepatitis A should be integrated into the national immunization schedule for children aged ≥ 1 year.

-In highly endemic countries, where natural immunity is acquired in young age, large-scale vaccination programmes are not recommended. In contrast, countries in transition from high to intermediate endemicity may experience an increased incidence of clinically significant disease and mortality from hepatitis A. In these settings, large-scale hepatitis A vaccination is likely to be cost-effective and is therefore encouraged. To control community-wide outbreaks, a single dose regimen of hepatitis A vaccine has been most successful when vaccination was started early and high coverage of multiple age-cohorts was achieved.

In low endemicity settings, targeted vaccination of high-risk groups should be considered. In certain risk groups such as the elderly or immunocompromised individuals, hepatitis A vaccines may be less efficacious and protection of shorter duration than in healthy young individuals.

Currently, inactivated HAV vaccines are licensed for intramuscular administration in a 2-dose schedule. Apart from a severe allergic reaction to the previous dose, there is no contraindication to their use. Inactivated hepatitis A vaccines should also be considered for pregnant women at definite risk of HAV infection.

Compared to the classical two-dose schedule, one single dose of inactivated hepatitis A vaccines is similarly efficacious, less expensive and easier to implement. Therefore, countries may consider the use of a single-dose schedule of this vaccine. However, in risk groups for hepatitis A, a two dose vaccination schedule is preferred.

The live attenuated vaccine is administered as a single dose. As a rule, live vaccines should not be used in pregnancy or in severely immunocompromised patients.

The use of hepatitis A vaccine rather than passive prophylaxis with immune globulin should be considered for both pre- and post-exposure prophylaxis.