Summary of WHO Position Paper on hepatitis A vaccines, October 2022

https://www.who.int/teams/immunization-vaccines-and-biologicals/policies/position-papers/hepatitis-a

This position paper, published in October 2022, replaces the corresponding WHO position paper on hepatitis A vaccines published in the Weekly Epidemiological Record in 2012.

Background

Hepatitis A virus (HAV) causes inflammatory liver disease that may progress in rare instances to fulminant liver failure. The virus is transmitted primarily via the faecal/oral route through ingestion of contaminated food and water, or through direct contact with an infectious person. The incidence of hepatitis A infection correlates with socioeconomic indicators, decreasing with increasing income, and access to clean water and adequate sanitation.

The clinical outcome is strongly correlated with age: while young children generally have asymptomatic infection, older children and adults commonly experience symptomatic disease. Likewise, mortality increases with age.

In 2019, Global Burden of Disease estimated 159 million acute HAV infections, resulting in 39 000 deaths and 2.3 million disability-adjusted life years.

Profiles of seroprevalence by age vary geographically. In most low-income regions, including sub-Saharan Africa and parts of south Asia, the prevalence of anti-HAV antibodies in the population may exceed 90% by the age of 10 years. In these areas, exposure to HAV usually occurs before the age of 5 years, when most HAV infections are asymptomatic. As a result of frequent childhood infections and consequent induction of lifelong immunity, there are few susceptible adolescents and adults, and hence little symptomatic disease. Outbreaks are rare in these regions.

In most high-income regions, the prevalence of anti-HAV antibodies is low but so is generally the risk also of acquiring HAV infection due to favourable socioeconomic conditions and hygienic practices.

In most middle-income regions of Asia, Latin America, Eastern Europe, and the Middle East, studies of anti-HAV antibodies in the population show a mix of intermediate and low prevalence. In these regions, where a substantial proportion of adolescents and adults are susceptible, HAV may circulate, often with regular community-wide outbreaks. HAV infection in adolescents and adults is associated with a higher rate of severe clinical manifestations. Thus, paradoxically, the transition from high to intermediate endemicity and a higher average age at infection is associated with an increase in the incidence of clinically significant hepatitis A disease.

Vaccines

The two types currently used are inactivated vaccines, and live attenuated vaccines, both highly immunogenic and efficacious at preventing clinical disease.

Inactivated hepatitis A vaccines are licensed for use in persons aged ≥12 months. According to the manufacturers, a complete vaccination schedule consists of two doses administered intramuscularly. A growing number of countries are using a paediatric single-dose (off label)
schedule. Effectiveness studies have demonstrated long-term protection with both two-dose or single-dose schedules. Inactivated vaccines have a very favourable safety profile.

Live attenuated hepatitis A vaccines are licensed for use in persons aged ≥18 months in a single-dose schedule. They are currently mainly used in China. The available body of evidence shows high efficacy and provide long-term protection. The safety profile is also favourable. But, as for other live attenuated vaccines, as a precautionary measure, they should not be given to pregnant women.

**WHO Position**

Vaccination against hepatitis A should be part of a comprehensive plan for the prevention and control of viral hepatitis, including measures to improve safe drinking-water, sanitation and hygiene (such as hand washing) and measures for outbreak control.

WHO recommends that vaccination against hepatitis A virus be introduced into national immunization schedules for individuals aged ≥12 months, if indicated on the basis of: i) an increasing trend over time of acute hepatitis A disease, including severe disease, among older children, adolescents or adults; ii) changes in the endemicity from high to intermediate; and iii) considerations of cost–effectiveness.

For children, inactivated hepatitis A vaccines can be given as a single- or two-dose (off-label) schedule, and administered intramuscularly. With a two-dose schedule, the first dose should be given starting from age ≥12 months. The interval between doses is flexible, from 6 months up to 4–5 years or more, but is usually 6–18 months.

For adults aged >40 years, vaccination with inactivated vaccines using the two-dose schedule is preferred since there is insufficient evidence on the immunogenicity and long-term protection from a single dose in this age group.

Live attenuated vaccines are licensed for individuals aged ≥18 months and are administered as a single subcutaneous dose.

In highly endemic countries, most individuals are asymptptomatically infected with HAV in childhood, which prevents clinical hepatitis A in adolescence and adulthood. In these countries, large-scale hepatitis A vaccination programmes are not routinely recommended, because they carry a risk of a paradoxical increase in disease incidence in unvaccinated people.

Countries with improving socioeconomic status may rapidly move from high to intermediate hepatitis A endemicity, rendering a larger proportion of the adolescent and/or young adult population susceptible to HAV infection. In such countries, large-scale hepatitis A vaccination in early childhood is likely to be cost–effective and is therefore recommended.

Targeted vaccination of high-risk groups should be considered in low and very low endemicity settings to provide individual health benefits.

In outbreak situations, single-dose hepatitis A vaccination is recommended, taking into account the epidemiology and feasibility of rapidly implementing a well-targeted vaccination programme.