

Hepatitis A vaccines

Summary of WHO Position Paper

WHO position paper on hepatitis A vaccines – October 2022

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Executive summary



World Health
Organization

- 1 **Hepatitis A infection causes inflammatory liver disease** that may progress in rare instances to fulminant liver failure
 - A. **Clinical outcome and mortality strongly correlated with age**: while young children generally have asymptomatic infection, older children and adults commonly experience symptomatic disease which may lead to severe illness and sometimes death.
 - B. **Disease burden** is estimated at **160 million cases** and **40000 deaths annually**
- 2 **Available hepatitis A vaccines are safe and highly effective and provide long-term protection** against symptomatic and severe disease.
- 3 **WHO recommends inclusion of hepatitis A in childhood immunization programmes 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.
 - A. **Single or two doses of inactivated vaccines** administered starting respectively at >12 months of age.
 - B. **Single dose of live attenuated vaccine** administered at >18 months of age.

1A Background of hepatitis A infection

- **Hepatitis A virus infections** causes inflammatory liver disease that may progress in rare instance to fulminant liver failure.
- **Transmission primarily via the faecal/oral route** through ingestion of contaminated food and water, or through direct contact with an infectious person.
- **Transmission associated with extensive shedding of the virus in faeces**, up to 6 months or longer **(for example, contact with a case within a household)**.
- **The incidence of hepatitis A infection correlates with socioeconomic indicators**, decreasing with increasing income, and access to clean water and adequate sanitation.
- **Clinical outcome strongly correlated with age**: while young children generally have asymptomatic infection, older children and adults commonly experience symptomatic disease.
- **Estimated 40 000 deaths per year**. Mortality increases with age (0.23% in under 30, to 2,1% in those aged >49 years).

Key take-aways

Hepatitis A infections, may in **rare** instance lead to **fulminant liver failure**, mainly in adults

1A Background of hepatitis A infection

Profiles of seroprevalence by age vary geographically

	Most low-income regions	Most high-income regions	Most middle-income regions
Prevalence of anti-HAV antibodies	High >90% by the age of 10 years	Low <50% by the age of 30 years	Mix of Intermediate or Low
Circulation of HAV/ risk of outbreaks	Low*	Low**	Increased***
Incidence of clinical significant disease , including severe disease	Low*	Low**	Increased***

*Due to few susceptible adolescents and adults left, and hence little symptomatic disease

**Due to favourable socioeconomic conditions and hygienic practices

***Due to substantial proportion of adolescents and adults are susceptible

Key take-aways

Hepatitis A severe infections **increase** with when countries **move** from **high to intermediate** endemicity

1B Disease, diagnosis and treatment

- **HAV** is **transmitted** primarily via the **faecal/oral route**. **Incubation period** of acute hepatitis A is usually **14–28 days**,
- **Symptoms** include **malaise, fatigue, anorexia, vomiting, abdominal discomfort, diarrhoea**.
- **Elevated levels of liver enzymes, dark urine and clay-coloured stools and jaundice** are characteristic manifestations of acute viral hepatitis.
- **Hepatitis A resolves completely in >99% of cases**, and does not cause chronic liver disease. **Immunity** is assumed **to persist for life**.
- Serological testing for **IgM anti-HAV** is required to establish the **etiological diagnosis of acute hepatitis A**. **HAV RNA** can be detected in body fluids and faeces and can persist for several months
- **Treatment** of hepatitis A is **mainly symptomatic**. In very rare instances of life-threatening liver failure, **hepatic transplant** might be required.
- **Incidence of hepatitis A infection correlates with socioeconomic indicators**, decreasing with increasing income, and access to clean water and adequate sanitation

Key take-aways

Hepatitis A infection is an **acute disease** it resolves spontaneously and results in life long immunity.

2 Hepatitis A vaccines

- **Two** different vaccines **types: Inactivated** and **Live attenuated** vaccines
- **Both vaccine types shown to be safe and highly effective** to protect against symptomatic infection
- **Inactivated vaccines** administered **intramuscularly** can be used in a **single- (off label) or two-dose schedule** from **12 months** onwards
 - **Both schedules** demonstrated **long-term protection (for up to 12 years)**, albeit the two-dose schedules resulting in higher GMCs compared to single-dose schedule
 - 2 WHO prequalified products
- **Life attenuated vaccines**, licensed as **single-dose** products and administered **subcutaneously** from **18 months** onwards, are mainly used in China
- Vaccines can be used effectively in **hepatitis A outbreak response**

Key take-aways

Currently available **hepatitis A vaccines** are **safe** and **effective** to **prevent symptomatic disease** in children and adults

2 WHO Position along 5 dimensions

A



Product choice & schedule

D



Vaccination of Special
Populations

B



Vaccine introduction
strategy

E



Surveillance & Research

C



Coadministration & special
contexts

2 Summary of 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**.
- Both **inactivated and live attenuated** hepatitis A vaccines are **safe** and **highly immunogenic**, and vaccination with either generates **long-lasting, possibly life-long, immunization** against hepatitis A in children, as well as in adults.
- For children, inactivated vaccines can be given **as a single- (off-label) or two-dose schedule**.

Key take-aways

Countries should include.

WHO Position- Product Choice and schedule

Inactivated vaccines

- For children, can be given **as a single- or two-dose 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**.
- Data on vaccine effectiveness, antibody persistence, and modelling on long-term seroprotection indicate that **an off-label, single-dose schedule is equivalent to the two-dose schedule in children**, in addition to being less costly and easier to implement.
- 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.
- **Inactivated** hepatitis A **vaccines** produced by different manufacturers, including combined hepatitis A vaccines, are **interchangeable**.
- Apart from **severe allergic** reaction to the previous dose, there are **no contraindications** to the use of **inactivated** hepatitis A vaccines.

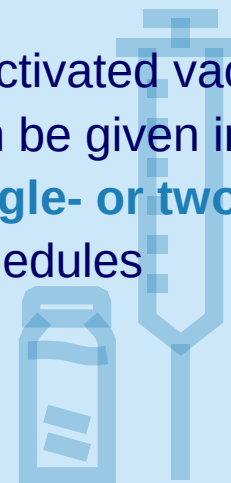
Live attenuated vaccines

- are licensed for individuals aged **≥18 months** and are administered as a **single subcutaneous** dose.
- Severe allergy to components included in the live attenuated hepatitis A vaccines is a contraindication to their use. **Live attenuated vaccines** may pose a theoretical risk to the developing foetus and therefore **should not be used during pregnancy**, nor should they be used in **severely immunocompromised patients**.

Key take-aways

Both **inactivated and live attenuated** hepatitis A vaccines are **safe and effective** and provide **long term** protection.

Inactivated vaccines can be given in **single- or two-dose** schedules

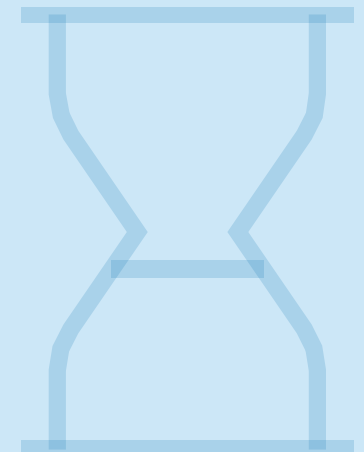


2B WHO Position- Vaccine introduction strategy

- **Choice of vaccination strategy** guided by
 - estimation of **country burden** of hepatitis A.
 - **age-specific prevalence of anti-HAV IgG antibodies** surveys,
 - **hepatitis A incidence**, associated **morbidity** and mortality.
 - These analyses need to be tailored to be able to detect **geographical variations**.
 - **Economic evaluation**, including **cost-effectiveness** of relevant immunization strategies, is a useful additional element for decision-making.
- In **highly endemic countries**,
 - most individuals are **asymptomatically 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**.
 - When introducing the vaccine, these countries should be based on **age-specific seroprevalence rates** or other markers of susceptibility.
- In **low and very low endemicity settings**
 - **Targeted vaccination** of **high-risk groups** should be considered to provide individual health benefits

Key take-aways

Hepatitis A vaccine **recommended** in countries **moving from high to intermediate hepatitis A endemicity**



2C WHO Position- Coadministration and special contexts

- **Co-administration**

- Hepatitis A vaccines can be administered simultaneously with any of the vaccines routinely used in childhood immunization programmes.

- **Special contexts**

- **Outbreaks**

- 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**. The use of hepatitis A vaccine to control outbreaks is most likely to be successful when the outbreak involves a **small self-contained community** or a **well-defined population**; when vaccination is **started early** in the course of the outbreak; and when high coverage of those likely to be affected can be achieved.

- **Pre and post exposure prophylaxis**

- **Hepatitis A vaccine** has largely **replaced immune globulin for pre- and post-exposure prophylaxis** due to having a similar efficacy and better safety profile, lower cost, wider availability and accessibility, and the advantage of providing longer persistent protection.

Key take-aways

Hepatitis A vaccines are **efficacious** in **outbreaks**, and **pre** and **post exposure prophylaxis**

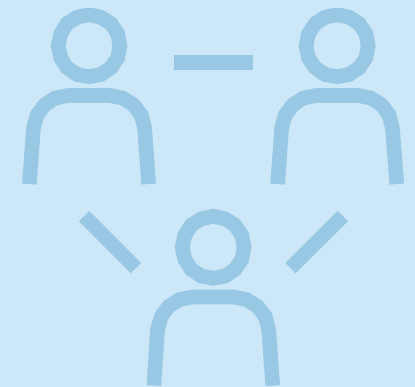


2D WHO Position- Vaccination of Special Populations

- Groups at higher risk of hepatitis A should be vaccinated, including **travellers** from low-endemic countries to areas of intermediate or high endemicity, **men who have sex with men**, at-risk **occupational groups**, people who **inject drugs**, people who experience **homelessness**, **migrants**, **refugees**, **incarcerated** persons; and patients with **chronic liver disease** or **HIV**, particularly **in countries with low and very low endemicity**
- For **immunocompromised individuals**, until further experience has been obtained with a single-dose schedule, a **two-dose schedule of inactivated vaccine is recommended**.
- Inactivated hepatitis A vaccines should also be considered for use in **pregnant women at risk of HAV infection**.
- **Health workers** are generally **not at special risk** of contracting hepatitis A and should follow the vaccine recommendations for the general population.

Key take-aways

High risk groups should be vaccinated in particular in **low endemicity settings**



2E WHO Position- Surveillance and Research Priorities

- Following the introduction of hepatitis A vaccines, it is important to **monitor**
 - **Impact** using **morbidity and mortality surveillance data**.
 - **Seroprotection**, and the duration of protection induced by **single- and two-dose schedules**
- **Modelling** studies are needed to
 - Characterize relationship between **levels of endemicity over time**, mean **age at infection**, and **increased risk of symptomatic and severe disease**
 - Guide countries on determining the **right timing** for **childhood vaccination introduction**.
- Data are needed on individuals who received a **single dose of inactivated vaccine during adult age** (rather than as children), particularly at **>40 years**, to confirm long-term protection.

Key take-aways

Monitoring and research is needed to fully understand **duration of protection** and characterise thresholds for **introduction**





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In case of additional questions, please reach out to the SAGE
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