

Summary of the WHO Position Paper on Vaccines against Japanese encephalitis (JE)

Background

This 2015 updated position paper on Japanese encephalitis (JE) vaccines replaces the 2006 JE position paper; it focuses on new information concerning the availability, safety, immunogenicity, and effectiveness of JE vaccines and the duration of protection they confer.

Japanese encephalitis (JE) is a vector-borne zoonotic viral disease. JE virus (JEV) is the leading cause of viral encephalitis in Asia. Currently, an estimated three billion people live in the 24 countries, mainly in the WHO South-East Asia and Western Pacific Regions, considered at risk of JE. It is estimated that 67 900 severe clinical cases of JE occur annually despite widespread availability of vaccine, with approximately 13 600 to 20 400 deaths. There is no specific antiviral treatment for JE. Most JEV infections are asymptomatic, and severe disease is estimated to occur in about one case per 250 JEV infections. While traditionally considered a childhood disease, JE can occur at all ages.

JE vaccines fall into four classes: inactivated mouse brain-derived vaccines, inactivated Vero cell-derived vaccines, live attenuated vaccines, and live recombinant (chimeric) vaccines. Protection against JEV is associated with the presence of sufficient levels of neutralizing antibodies. The accepted immunological surrogate of protection is a serum neutralizing antibody titre of at least 1:10 as determined in a 50% plaque reduction neutralization assay (PRNT₅₀). The available evidence demonstrates that all four classes of vaccines elicit protective levels of neutralizing antibody. Vaccine effectiveness data for live attenuated vaccine suggest over 95% effectiveness five years post-vaccination. The WHO Global Advisory Committee on Vaccine Safety (GACVS) has reviewed data on two inactivated Vero cell-derived vaccines, the live attenuated vaccine and the live recombinant vaccine, and all were found to have acceptable safety profiles. Available data do not raise concerns for those previously vaccinated with mouse brain-derived vaccine subsequently receiving any of the three newer JE vaccines.

Data on the population impact of vaccination programmes show significant reductions in JE cases. When high coverage is achieved and sustained in populations at risk of disease, JE in humans can be virtually eliminated while the virus remains in circulation in animal reservoirs. It has been demonstrated that a variety of JE vaccination strategies are cost-effective or highly cost-effective.

WHO Position

JE vaccination should be integrated into national immunization schedules in all areas where JE is recognized as a public health priority. Even if the number of JE-confirmed cases is low, vaccination should be considered where there is a suitable environment for JEV transmission. Adjunctive interventions, such as bednets and mosquito control measures, should not divert efforts from childhood JE vaccination.

The most effective immunization strategy in JE endemic settings is a one-time campaign in the primary target population, as defined by local epidemiology (typically children aged <15 years), followed by incorporation of JE vaccine into the routine childhood immunization programme. This approach has a greater public health impact than either of these approaches alone, as campaigns rapidly reduce disease incidence in a broader age group of susceptible individuals. Older groups may be considered for vaccination if the disease burden in such groups is sufficiently high.

The following vaccine dosing schedules and ages of administration are recommended:

- Inactivated Vero cell-derived vaccine: Primary series according to manufacturer's recommendations (these vary by product), generally 2 doses at 4-week intervals starting the primary series at ≥ 6 months of age in endemic settings
- Live attenuated vaccine: Single dose administered at ≥ 8 months of age
- Live recombinant vaccine: Single dose administered at ≥ 9 months of age

The need for a booster dose in endemic settings has not been clearly established for any of the vaccines listed above. Preferably, inactivated mouse brain-derived vaccines should be replaced by these newer generation JE vaccines.

Despite a lack of comprehensive immunogenicity/effectiveness and safety data for all possible combinations of JE and other routine vaccines, co-administration for programmatic reasons seems acceptable, even in the context of mass campaigns.

Strengthened surveillance is needed to assess the burden of JE, inform vaccination strategies, identify breakthrough cases, monitor vaccine safety, and monitor the impact and effectiveness of JE vaccines and assess the potential need for booster doses to close gaps in immunity. All JE-endemic countries are encouraged to carry out at least sentinel surveillance with laboratory confirmation of JE.

Long-term immunogenicity studies are needed to inform optimal dosing schedules for long-term protection, which may vary by location (based on natural boosting or other factors). Vaccine effectiveness and impact studies are also important.