Adverse Event

Global Advisory Committee on Vaccine Safety, 910 June 2005

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GACVS was advised that there is no definite evidence of an increased risk of acute disseminated encephalomyelitis temporally associated with JE vaccine and a causal link has not been demonstrated.

The national authority recommends vaccination in high-risk areas only and for travel to endemic regions.

GACVS concluded, on the information presently available, that there is no good reason for WHO and national immunization programmes to change the current recommendations for JE vaccination for residents in and travellers to JE-endemic regions.


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GACVS acknowledged the excellent safety and efficacy profile of the (live attenuated) SA 14-14-2 (Japanese encephalitis) vaccine but nonetheless recommended more detailed study of the following: the safety profile in special risk groups including immunocompromised people and pregnant women; whether viral shedding occurs in vaccinees and the potential implications of such shedding; further analysis of sequential or co-administration of JE and measles vaccines; the interchangeability of inactivated and live JE vaccines; the safety of vaccine administration to infants aged under 1 year; and the implications for the efficacy and safety of the vaccine in infants with maternal antibodies against JE virus.

General

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The national authority recommends vaccination in high-risk areas only and for travel to endemic regions.

GACVS concluded, on the information presently available, that there is no good reason for WHO and national immunization programmes to change the current recommendations for JE vaccination for residents in and travellers to JE-endemic regions.

Further studies are needed to document the safety of administering Japanese encephalitis (JE) vaccine concomitantly with the measles vaccine. If the first dose of JE vaccine could be given at the same visit with the first dose of measles, this will fit better into the schedule of the national immunization programme (NIP) and may help to increase coverage.

In countries having a good surveillance and laboratory framework, impact of JE vaccination on other flavivirus infections should be monitored.

SAGE recommended that surveillance (for Japanese encephalitis) be conducted in accordance with the established WHO surveillance standards* and that sentinel sites be equipped to confirm diagnosis using validated and standardized diagnostic tests. There is a need to establish disease surveillance in rural areas. SAGE recommended that commercial kits for detection of JE-specific IgM be compared and validated. SAGE noted that valuable experience had been gained from linking surveillance of encephalitis to detection of acute flaccid paralysis.


SAGE commended the efforts of countries (regarding Japanese encephalitis control) and acknowledged that immunization is the most appropriate means of controlling the disease. It also acknowledged the cost-effectiveness of the measure.

SAGE recommended that (Japanese encephalitis) immunization strategies be guided by evidence of the burden of disease, the impact and safety of immunization and the ability to integrate JE vaccination into the EPI programme.

Interference with the immune response to other vaccinations, the number of doses required and the duration of protection need to be assessed. Efforts to continue measuring incidence of acute encephalitis syndrome and to confirm diagnoses need to be sustained.

SAGE requested the updating of the WHO position paper on JE immunization.
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, i.e. presence of animal reservoirs, ecological conditions supportive of virus transmission, and proximity to other countries or regions with known JEV transmission.

Adjunctive interventions, such as bednets and mosquito control measures, should not divert efforts from childhood JE vaccination.

As JE vaccination does not induce herd immunity, high vaccination coverage should be achieved and sustained in populations at risk of the disease.

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.

If an outbreak occurs in a country or region where JE vaccination has not been introduced, an assessment needs to be made of whether it is appropriate to implement an immediate vaccine response. Single-dose live attenuated or live recombinant vaccines should be used when reactive vaccination campaigns are implemented during an outbreak. When outbreak response vaccination is conducted, planning for introduction into the routine immunization schedule should follow.

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 would be accepted.
When possible, campaigns should be scheduled outside periods of high JE disease activity, to prevent as much disease as possible in advance of high transmission and to reduce suspicion of a relationship between encephalitis cases and vaccination.

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

- Inactivated Vero cell-derived vaccine: Primary series according to manufacturers 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 inactivated Vero-cell-derived, live attenuated or live recombinant vaccines.

Preferably, inactivated mouse brain-derived vaccines should be replaced by the 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 would be accepted, even in the context of mass campaigns.

Due to the need for rapid production of protective antibodies, single-dose live attenuated or live recombinant vaccines should be used when reactive vaccination campaigns are implemented in the context of an outbreak.

When outbreak response vaccination is conducted, planning for introduction into the routine immunization schedule should follow.
Inactivated Vero cell-derived vaccines should be used preferentially over live attenuated or live recombinant vaccines in immunocompromised persons. HIV testing is not a prerequisite for vaccination.

For the vaccination of pregnant women, inactivated Vero cell-derived vaccines should be used preferentially over live attenuated or live recombinant vaccines based on the general precautionary principle against using live vaccines in pregnant women especially if alternative types of vaccines are available.

Pregnancy testing is not a prerequisite for JE vaccination.

Inadvertent administration of live attenuated or live recombinant JE vaccine to a pregnant woman is not an indication for termination of the pregnancy.

Workers at high-risk in endemic areas, such as those involved in vector control, should be vaccinated.

JE vaccination is recommended for travellers to endemic areas with extensive outdoor exposure during the transmission season.

For inactivated Vero cell-derived vaccines, data support a booster dose at >1 year in adults travellers following the primary schedule if at risk of further exposure to JEV. For live recombinant vaccine, currently available data in adults do not suggest a need for a booster dose for travellers. There are no long-term data publically available for either vaccine administered to children in non-endemic settings.

Migrants to JE-endemic areas should be vaccinated.

All JE-endemic countries are encouraged to carry out at least sentinel surveillance with laboratory confirmation of JE.
While a comprehensive JE surveillance system is recommended, countries without a strong system in place but with evidence of JE disease occurrence should not wait to introduce JE vaccine.

Given the burden of disease in adults in some countries, consideration should be given to capturing cases in all age groups in the surveillance system.

Further developments of sensitive, specific, affordable commercial serological assays to ensure access to diagnostic testing in JE-endemic countries should be advanced.

New Vaccines

Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

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SAGE recommended that (Japanese encephalitis) immunization strategies be guided by evidence of the burden of disease, the impact and safety of immunization and the ability to integrate JE vaccination into the EPI programme.

Interference with the immune response to other vaccinations, the number of doses required and the duration of protection need to be assessed. Efforts to continue measuring incidence of acute encephalitis syndrome and to confirm diagnoses need to be sustained.

Policy

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

Further studies are needed to document the safety of administering Japanese encephalitis (JE) vaccine concomitantly with the measles vaccine. If the first dose of JE vaccine could be given at the same visit with the first dose of measles, this will fit better into the schedule of the national immunization programme (NIP) and may help to increase coverage.
In countries having a good surveillance and laboratory framework, impact of JE vaccination on other flavivirus infections should be monitored.

### Pregnant Women

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### Program Management

**Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006**

SAGE requested the updating of the WHO position paper on JE immunization.

### Research

**Global Advisory Committee on Vaccine Safety, 910 June 2005**

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**SAGE - recommend to WHO**

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**Travellers**

Global Advisory Committee on Vaccine Safety, 9-10 June 2005

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**VPD Surveillance**

Vaccine introduction guidelines. Adding a vaccine to a national immunization programme: decision and implementation

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Conclusions and recommendations from the Strategic Advisory Group of Experts (SAGE) - 10-11 April 2006

SAGE recommended that surveillance (for Japanese encephalitis) be conducted in accordance with the established WHO surveillance standards* and that sentinel sites be equipped to confirm diagnosis using validated and standardized diagnostic tests. There is a need to establish disease surveillance in rural areas. SAGE recommended that commercial kits for detection of JE-specific IgM be compared and validated. SAGE noted that valuable experience had been gained from linking surveillance of encephalitis to detection of acute flaccid paralysis.