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Japanese encephalitis surveillance

Introduction

Japanese encephalitis (JE) is caused by the JE virus. In temperate and tropical regions of Asia, the virus is maintained through a transmission cycle between vertebrate amplifying hosts (e.g. pigs, herons, egrets) and several Culex mosquito species. JE virus is the leading cause of encephalitis in Asia. Human vaccination has proven to be the single most effective preventive intervention against JE. JE surveillance is essential for monitoring the effectiveness of the vaccine and measuring the degree of control achieved by the local immunization programme.

Since clinical grounds alone do not suffice to distinguish JE from encephalitis due to other causes, a syndromic approach is used for the identification of cases. Acute encephalitis syndrome (AES) surveillance is conducted to characterize the epidemiology and burden of the disease, identify high-risk areas requiring an appropriate public health response and document the impact of control measures. For several reasons, sentinel hospital-based surveillance is more practical than general passive surveillance. First of all, in many countries, especially large ones, JE may be confined to certain geographical regions. Second, laboratory confirmation is necessary to confirm the aetiology of the virus, but the required facilities may not be widely available.

Objectives

The objectives of JE surveillance are to:

- understand the epidemiology of JE, including the definition of the populations at risk and estimation of the disease burden in the country;
- determine the geographical distribution of JE in the country;
- provide information for the formulation of a vaccination policy; and
- evaluate the impact and effectiveness of the vaccine after its introduction.

Types of surveillance

Sentinel hospital-based surveillance: This type of surveillance is indicated in areas where JE is suspected to be a health issue. The sentinel sites in a geographical area should initially consist of the hospitals with the largest input of suspected cases, and the sites can be increased when feasible. The criteria for the strategic selection of sentinel sites should be based on their representativeness within the geographical region(s), and should also include the following:
• the risk profile for JE, e.g. if it is located in a JE-endemic area and if it serves as a referral centre for encephalitis patients;
• the size of the health facility and the access of the catchment population; and
• the capability of the health facility staff to carry out active encephalitis case detection and the feasibility of specimen collection and testing.

When a country has achieved a high level of control of JE, surveillance should be case-based throughout the country and should include laboratory confirmation of all reported cases.

**Nationwide case-based surveillance:** Nationwide, case-based surveillance for JE and AES might be useful in the following ways, though it requires extensive resources:

• Data from nationwide surveillance of AES, with laboratory confirmation, constitute the best source of information on the complete disease burden of JE.
• Nationwide surveillance in all hospitals, with laboratory confirmation of all suspected cases, can capture the maximum cases in countries where a high level of control of JE has been achieved.

**Age group for surveillance:** Surveillance for JE is recommended for all age groups for the following reasons:

• Though JE is commonly found to affect children younger than 15 years of age in Asia, cases can occur among the older age groups too, especially when the virus enters a new area.
• In areas with a JE vaccination programme, the proportion of cases frequently rises among older, unvaccinated age groups.

While it is recommended that surveillance should include all age groups, in countries that are in the early stage of implementing a JE vaccination programme, it is cost-effective to conduct surveillance among children < 15 years of age, or in the group with the preponderance of cases.

**Case detection**

**Definition of suspected case**

• A suspected JE case is a person whose condition matches the definition of AES. The clinical case definition of AES refers to a person of any age who, at any time of the year, develops a fever of acute onset and at least one of the following:
a change in mental status (including symptoms such as confusion, disorientation, coma or inability to talk); or
new onset of seizures, excluding simple febrile seizures. A simple febrile seizure is defined as a seizure among children who are between 6 months and 6 years of age, in whom the only findings are fever and a single generalized convulsion lasting less than 15 minutes, and who recover consciousness within 60 minutes of the seizure.

Sensitivity and specificity of definition
The definition of a suspected AES case has high sensitivity but low specificity. It might have reduced sensitivity for JE among children in some settings. Overall, the AES case definition has been seen to capture two-thirds of children with JE; it had 100% sensitivity among adults, though the numbers were small.

Case description
The illness usually begins with fever of sudden onset, headache and vomiting. Among children, gastrointestinal pain and vomiting may be the dominant initial symptoms. Changes in mental status, focal neurological deficits, generalized weakness and movement disorders may develop over the next few days. The classical description of JE includes a mask-like face, tremor, muscular stiffness and involuntary (choreoathetoid) movements. Acute flaccid paralysis, with clinical features similar to those of poliomyelitis, has also been associated with JE. Seizures are common, especially among children.

Differential diagnosis
Acute disease with impaired brain function may have other causes as well, such as:
- meningitis (viral and bacterial, including tuberculosis);
- encephalopathy due to toxins;
- cerebral malaria;
- viral encephalitis due to herpes simplex virus, mumps virus or neurovirulent enteroviruses (e.g. enterovirus 68 or enterovirus 71 with hand, foot and mouth syndrome); and
- or post-infectious meningoencephalitis (e.g. post-measles or post-varicella).

Date of onset of illness
The date of onset of JE should be considered as the date of onset of the first sign/symptom of AES.
Response to suspected case

Case reporting

The sites most likely to report cases are sentinel hospitals where AES cases are expected to be seen and admitted. All suspected JE cases must be reported to the district surveillance officer. The on-site staff is responsible for collecting specimens for laboratory tests.

Investigation of suspected case

Once the health-care staff has identified a case according to the criteria of AES, it must fill in a case investigation form and draw specimens for laboratory testing.

Case investigation form

A case investigation form should be filled for every suspected case within 48 hours of reporting. (See Annex 2 for a sample case investigation form.)

Unique ID

A unique case identification number (UID) should be assigned to each suspected case. The number should begin with one or more three-letter combinations that designate the geographical location, followed by the year and the serial number of the case. All communications and forms related to the case should cite the UID.

For example:
- AES – suspected AES code
- THA – country code
- BKK – province code
- BBN – district code
- 2022 – year of onset
- 001 – serial number of JE case in the province

The UID would then be AES-THA-BKK-BBN-22-001.

Specimen collection

Types of specimens

The preferred specimen for laboratory confirmation is cerebrospinal fluid (CSF), obtained through a lumbar puncture, to test for JE virus-specific IgM antibody. JE virus-specific IgM
can be measured in the CSF of most patients by 4 days of the onset of symptoms.

If facilities for a lumbar puncture are not available, blood samples should be collected soon after admission to test for JE virus-specific IgM. The antibody can be measured in the serum by 7 days of the onset of symptoms.

**How much to collect**

- **Cerebrospinal fluid:**
  - At least two tubes should be sent to the hospital laboratory for microbiology (Gram stain and bacterial culture), and the estimation of CSF glucose, protein and cell count. The results of these tests will assist with the diagnosis and clinical management of the patient.
  - If facilities for JE testing are not available at the sentinel hospital, another tube of CSF should be sent to the national or regional reference laboratories for JE-specific testing.
- Amount of blood sample to be sent to the laboratory:
  - 3–5 mL of blood for older children and adults; and
  - 1–2 mL of blood for infants and younger children.

**Storage and transport**

- If the specimens can be transported within 1–3 days, the CSF and serum samples should be stored at 2–8 °C in a refrigerator.
- For longer term storage, specimens should be stored at or below -20 °C.
- As a general rule, repeated freezing and thawing of samples should be avoided. Therefore, it is important to store them at the appropriate temperature.

**Indications for a second blood sample**

If the first CSF or blood sample is positive for JE IgM, it is not necessary to test a second sample. However, the IgM ELISA test is more often than not conducted at a location that is different from where the sample was collected (such as a national laboratory or provincial laboratory). This means a prolonged specimen transport and testing time, and the results are often not available till the patient’s discharge or death. Therefore, it is good clinical practice to collect a second sample of blood as well.

If JE-specific IgM antibodies are not be present when the first blood sample is taken, a second blood sample must be obtained:

- on day 10 of the illness (usually on the seventh day of hospitalization);
- at the time of discharge; or
- at the time of death.
Laboratory testing

Recommended method of laboratory confirmation

For laboratory confirmation, the JE virus IgM antibody test needs to be conducted. An IgM capture ELISA specifically for JE virus may be used to detect the presence of the JE virus-specific IgM in a single sample of CSF or serum. The sensitivity to the antibodies increases to > 95% in 10 days after the onset of the initial symptoms.

It is important to differentiate true JE virus infections from other infections that yield false-positive JE results because of cross-reactive epitopes among flaviviruses. To cite an example, a patient with a dengue virus infection might have a positive JE IgM result because of flavivirus cross-reactivity. The current commercial assays for the detection of JE IgM have low specificity for JE. Therefore, to rule out false-positive results, a validated dengue-specific assay has to be carried out on all JE-positive specimens.

In addition, JE can be confirmed by any of the following:

- detection of JE virus antigens in brain tissue by immunohistochemistry or immunofluorescence assay;
- detection of the JE virus genome in CSF, serum, plasma, blood or brain tissue by reverse transcription polymerase chain reaction (RT-PCR) or an equally sensitive and specific nucleic acid detection assay, such as loop-mediated isothermal amplification or whole genome sequencing;
- isolation of the JE virus in CSF, serum, plasma, blood or brain tissue;
- detection of a fourfold or greater rise in JE virus-specific IgG antibody as measured by the plaque reduction neutralization test (PRNT) in serum collected during the acute and convalescent phases of the illness (the two specimens should be collected at least 14 days apart).

Interpretation of IgM antibodies test

- Positive:
  - IgM antibodies usually persist for 30–90 days and in a few cases, for longer periods as well. Therefore, a positive result for IgM antibodies occasionally reflects a past infection or vaccination.
  - In areas highly endemic for JE, it is possible for a patient to have AES due to other causes, but to have JE virus-specific IgM antibody present in the
serum from a recent, possibly subclinical infection. Therefore, all persons with encephalitis are advised to have a CSF sample tested, if feasible. Even in the presence of a positive CSF specimen, further confirmatory tests should be carried out (such as looking for cross-reactivity with other flaviviruses circulating in the geographical area) in any of these situations:

- if there is an ongoing dengue or other flavivirus outbreak;
- if the coverage of JE vaccination is very high; and
- if the area does not have epidemiological and entomological data supportive of JE transmission.

- For persons vaccinated with the JE vaccine within 6 months prior to the onset of illness, testing a single serum sample for JE IgM may not be diagnostic because any IgM detected may be vaccine-related. In such cases, a diagnosis can be confirmed only by:
  - detection of JE IgM in the CSF;
  - isolation of the JE virus;
  - a positive nucleic acid amplification test;
  - immunohistochemistry; or
  - a fourfold or greater rise in antibody titre between acute- and convalescent-phase serum samples.

- Negative:

Serum collected in the initial days of the illness (before 7 days of onset) may not have detectable IgM. In such cases, the test should be repeated on a convalescent-phase serum sample.

A fourfold or greater rise in JE virus-specific antibodies between acute- and convalescent-phase serum specimens may be used to confirm recent infection. When interpreting results, it is necessary to consider the person’s vaccination history, the date of onset of the symptoms, and information regarding other flaviviruses known to circulate in the geographical area that may cross-react in serological assays.

Virus isolation and nucleic acid amplification tests should not be used for ruling out a diagnosis of JE as they are insensitive in detecting JE virus or viral RNA in blood or CSF, since humans have a low level of viraemia.

An examination of the CSF, including the cell count, cell morphology and standard biochemistry, can distinguish between encephalitis and encephalopathy and between encephalitis and meningitis, as shown in Table 10.1.
Table 10.1: CSF examination results and conditions indicated

<table>
<thead>
<tr>
<th>Result</th>
<th>Indicative of</th>
</tr>
</thead>
<tbody>
<tr>
<td>CSF cell count &lt; 10 cells/mm³, and especially &lt; 6 cells/mm³</td>
<td>Encephalopathy or early bacterial infection</td>
</tr>
<tr>
<td>CSF cell count of 10–100 cells/mm³, predominantly lymphocytic</td>
<td>Encephalitis or viral meningitis</td>
</tr>
<tr>
<td>CSF cell count &gt; 100 cells/mm³ with predominantly polymorphs</td>
<td>Bacterial meningitis</td>
</tr>
<tr>
<td>CSF cell count &gt; 100 cells/mm³ with predominantly lymphocytes</td>
<td>Viral meningitis</td>
</tr>
</tbody>
</table>

A high protein concentration (> 100 mg/dL) and low glucose (< 40 mg/dL) may indicate tuberculous meningitis or another bacterial cause.

Classification of cases

**Laboratory-confirmed case**

A laboratory-confirmed case is a suspected case that has been confirmed in the laboratory as being one of JE.

**Probable JE**

This is a suspected case that occurs in close geographical and temporal relationship to a laboratory-confirmed case of JE, in the context of an outbreak.

**AES – other agent**

This refers to a suspected case in which diagnostic testing was performed and an aetiological agent other than JE virus was identified.

**AES – unknown**

This refers to a suspected case in which no diagnostic testing was performed or in which testing was performed but no aetiological agent was identified, or in which the test results were indeterminate.
JAPANESE ENCEPHALITIS

Caveats

- JE cannot be ruled out in cases with IgM-negative results if the sample was collected less than seven days after the onset of illness because the IgM may not have risen to detectable levels, and a second sample should be collected.
- The detection of the virus genome or isolation of the virus in serum, plasma or blood is very specific for the diagnosis of JE; however, it is not sensitive, as virus levels are usually undetectable in clinically ill JE cases. Therefore, a negative result by these methods should not be used to rule outJE in a suspected case.
- It is usually in fatal cases that the virus genome is detected or the virus isolated in CSF. Therefore, these methods are not very sensitive and should not be used for ruling out a diagnosis of JE.

Fig. 10.1: Classification of AES cases

Final classification scheme for AES cases

- Adequate Blood / CSF sample
  - IgM Positive
    - +VE: Lab confirmed JE
    - -VE: AES Other agent
- AES (suspected JE)
  - IgM negative
    - Geographic / Temporal link to a lab confirmed JE case during an outbreak
      - No geographic / temporal link to a lab confirmed JE case: AES unknown
- No / Inadequate Blood / CSF sample
  - AES unknown

Source: WHO manual for the laboratory diagnosis of Japanese encephalitis virus infection, 2007

Contact tracing

Contact investigations are not carried out for JE as the disease is vector-borne.
Clinical management

- No specific antiviral treatment has been found to benefit patients with JE.
- As in other AES cases, the patient generally requires hospitalization for supportive care and close observation.
- Special supportive care should be provided if any of the following potentially life-threatening, preventable complications is detected:
  - raised intracranial pressure
  - status epilepticus
  - hypoglycaemia
  - aspiration pneumonia
  - secondary infections.
- Normal supportive care includes rest, intake of fluids and pain relievers and medication to reduce fever. The administration of intravenous fluids and vasopressors might be needed in severe cases.

Outbreak

Definition

An outbreak is an occurrence of the disease in excess of the expected frequency in a given area among a specific group of people over a particular period of time, or of two or more epidemiologically linked cases in a short period.

Major outbreaks occur every 2–15 years in endemic areas, especially those where the use of the JE vaccine is not widespread. The transmission of the virus usually intensifies during the rainy season, when vector populations increase. Studies have shown a strong association between agricultural practices, including rice cultivation, and the density of the vector mosquitoes. Therefore, an increase in the abundance of rice fields or the establishment of rice cultivation in new areas is likely to increase the risk of JE.

Modifications needed in surveillance

- Only the first 5–10 cases of an outbreak need to be confirmed through laboratory testing.
- If an outbreak continues over a protracted period of time, another 5–10 samples should be collected every 2–3 months to ascertain whether it is still JE that is causing the outbreak.
- If the outbreak is not an expected seasonal one, or there are unusual epidemiological features (such as the age distribution of cases not being consistent with the pattern of JE infection or the absence of typical vectors or hosts), it is especially important to test CSF samples, as an encephalitis outbreak can have other causes.
DATA MANAGEMENT

JAPANESE ENCEPHALITIS

Data management

Reporting requirements
Aggregate case counts (confirmed and probable) to track the disease burden are sufficient to identify clusters and monitor trends.

- Aggregate case counts should be reported to the public health authorities at least once a month.
- In countries where a high level of JE control has been achieved, case-based data should be reported. Reporting should be weekly or monthly, and must include “zero reporting” (i.e. a zero should be written when no cases have been detected, leaving no blanks in the reporting forms).
- Although the International Health Regulations do not require the reporting of JE cases, JE is included in the World Health Organization (WHO)/United Nations Children’s Fund Joint Reporting Form, which should be submitted annually.

Unique ID
A unique case identification number should be assigned to each suspected case, as explained earlier.

Recommended data elements
- Unique case identifier
- Date of birth (or age, if date of birth is not available)
- Sex
- Place of residence (city, district and province)
- Travel history over the past two weeks
- If ever immunized against JE
- Number of vaccine doses received
- Dates of vaccine doses (if available)
- If vaccinated, type of vaccine received most recently
- Symptoms (fever, change in mental status, seizure)
- Date of onset of first symptoms
- Type of specimen collected (CSF, serum, autopsy)
- Type(s) of testing methodology (IgM, PRNT, PCR, virus isolation, etc.)
- Date(s) of specimen collection (including serum samples 1 and 2)
- Date(s) of receipt of specimen(s) in laboratory
- Date(s) of testing of specimen(s) (for each type of test)
Surveillance Guide for vaccine-Preventable Diseases in the WHO South-East Asia Region

- Date(s) on which laboratory reported results
- Laboratory results for each specimen
- Final classification: laboratory-confirmed JE, probable JE, AES-unknown, AES-other agent
- Status at discharge: alive, dead, unknown
- Date of death or discharge

These data elements have been put together in the sample case investigation form (Annex 2).

Data analysis

- Number of suspected cases by week, month, year, age group and geographical area
- Number of confirmed cases by week, month, year, age group and geographical area
- Number of deaths due to JE
- Coverage of JE vaccine by year and geographical area
- Percentages of vaccinated and unvaccinated cases, and completeness/timeliness of monthly reporting by geographical area
- Suspected and confirmed cases – incidence specific to age, gender, geographical area and immunization status
- Percentage of suspected cases whose CSF and/or serum specimens were collected
- Percentage of cases whose serum sample was collected 10 or more days after the onset of illness (when testing methodology was IgM-capture ELISA)
- Case fatality ratio
- Final classification of all suspected cases
- Proportion of AES attributed to JE

Using data for decision-making

Surveillance data on JE may be used to:

- guide policy and strategies on the control of JE;
- assess the impact of vaccination;
- identify geographical areas or populations at high risk to provide further guidance on where the coverage of immunization should be improved;
- monitor the performance of surveillance;
- monitor the performance of laboratories; and
- monitor the effectiveness of vaccines.
### Surveillance performance

Table 10.2 shows the indicators and targets for evaluating the performance of a surveillance system. The targets are for countries with a well-established AES surveillance system.

**Table 10.2: Indicators for surveillance performance**

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Indicator</th>
<th>Target</th>
<th>How to calculate</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Completeness of reporting</td>
<td>Proportion of surveillance units reporting to the national level, even in the absence of cases</td>
<td>≥ 80%</td>
<td>(Number of surveillance units reporting / number of surveillance units in the country) x 100</td>
<td></td>
</tr>
<tr>
<td>Timeliness of reporting</td>
<td>Proportion of surveillance units reporting to the national level on time, even in the absence of cases</td>
<td>≥ 80%</td>
<td>(Number of surveillance units reporting by the deadline / number of surveillance units in the country) x 100</td>
<td>Note 1</td>
</tr>
<tr>
<td>Specimen collection</td>
<td>Proportion of all suspected cases for which at least 1 specimen was collected</td>
<td>≥ 90%</td>
<td>(Number of AES cases with specimen collected / number of AES cases) x 100</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Proportion of suspected AES cases who had a lumbar puncture performed</td>
<td>≥ 90%</td>
<td>(Number of suspected AES cases who had a lumbar puncture performed / number of suspected AES cases) x 100</td>
<td>None</td>
</tr>
<tr>
<td></td>
<td>Proportion of serum samples taken a minimum of 10 days after onset of illness</td>
<td>≥ 80%</td>
<td>(Number of serum samples obtained at least 10 days after onset of illness / number of serum samples received by laboratory) x 100</td>
<td>Note 2</td>
</tr>
<tr>
<td>Specimen adequacy</td>
<td>Proportion of CSF and serum samples reaching laboratory in adequate condition</td>
<td>≥ 80%</td>
<td>(Number of CSF and serum samples reaching laboratory in adequate condition / all CSF and serum samples received by laboratory) x 100</td>
<td>Note 3</td>
</tr>
</tbody>
</table>
### Attribute Indicator Target How to calculate Comments

<table>
<thead>
<tr>
<th>Attribute</th>
<th>Indicator</th>
<th>Target</th>
<th>How to calculate</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timeliness of reporting laboratory results</td>
<td>Proportion of laboratory results reported to national public health authorities 7 days after receipt of specimen</td>
<td>≥ 80%</td>
<td>(Number of laboratory test results reported &lt; 7 days after receipt of specimen / number of specimens received by laboratory) x 100</td>
<td>Note 4</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>Minimal AES rate per 100 000 population</td>
<td>&gt; 2/100 000</td>
<td>(Number of AES cases captured by surveillance / number of target population in the country) x 100 000</td>
<td>Note 5</td>
</tr>
</tbody>
</table>

**Notes**

- The reporting should be at least quarterly. At each level, reports should be received on or before the requested date.
- This applies to laboratories where the testing methodology is IgM capture ELISA.
- To be “adequate”: (a) the specimen should be transported using reverse cold chain, and (b) the sample volume must be greater than 100 µL.
- This indicator applies only to public laboratories.
- This applies to enhanced (nationwide) surveillance and not minimal (sentinel) surveillance.

---

**Public health response**

The public health response to JE should include the following.

**Vaccination**

JE vaccination should be integrated into national immunization schedules in all areas where the illness is recognized as a public health priority.

**Health education and community involvement**

Community awareness helps to shorten the delay between the onset of symptoms and the time of seeking medical care. Immediate supportive management of cases helps to cut down deaths.

** Interruption of transmission**

Vaccination of humans is the only proven method for reducing JE disease. There is little evidence to support the vaccination of pigs, environmental management for vector control, and chemical control of vectors.
Annex 1: Disease epidemiology

Background

Japanese encephalitis is an infection of the brain/central nervous system, caused by a flavivirus. JE virus (JEV) is transmitted to humans through the bite of infected mosquitoes of the *Culex* species, particularly *Culex tritaeniorhynchus*. The virus is maintained in nature via a cycle between mosquitoes and vertebrate hosts, primarily pigs and water birds. Humans are infected incidentally and are dead-end hosts as they are unable to pass on the infection. This is because they usually do not develop high enough concentrations of the virus in their bloodstream to infect mosquitoes feeding on them. The virus has five genotypes.

Most infected people are asymptomatic. Therefore, it is difficult to determine the accurate incidence of JE and the disease burden may be underestimated. It is estimated that less than 1% of humans infected by JEV develop disease.

Japanese encephalitis is a disease of great public health concern due to its severe morbidity and mortality and the continuing increase in its global distribution. It is the leading cause of tropical viral diseases. At present, most cases are being reported from the WHO South-East Asia Region (almost 60%) and Western Pacific Region (about 40%).

Though most JEV infections either have no symptoms or mild (fever and headache) or short-lived ones, approximately 1 in 250 infections results in severe clinical illness. Severe disease is characterized by the rapid onset of a high fever, headache, stiffness of the neck, change in mental status/disorientation, coma, fits/convulsions (common among children), weakness in the limbs, spastic paralysis and ultimately, death. The case fatality rate can be as high as 30% among those with symptoms, the number of deaths amounting to approximately 13 600–20 400 annually. Of those who survive, 20–30% suffer permanent intellectual, behavioural or neurological sequelae, such as paralysis, recurrent seizures and the inability to speak.

Essential epidemiology

*Infectious agent:* The Japanese encephalitis virus is a flavivirus.

*Reservoir of infection:* The virus is maintained in a cycle between mosquitoes and pigs and water birds.
Mode of transmission: JE is transmitted through the bite of an infected mosquito belonging to the Culex species.

Incubation period: 5–15 days

Period of communicability: Humans are generally a dead-end host and do not infect mosquitoes.

Case fatality ratio: Up to 30% among those with severe clinical symptoms

Vaccines

The four main types of JE vaccines currently in use are shown in Table 10. A1.

Table 10. A1: JE vaccines and doses

<table>
<thead>
<tr>
<th>Type of vaccine</th>
<th>Number of doses</th>
<th>Age at which to be administered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inactivated mouse brain-derived vaccines</td>
<td>Production halted in 2006, remaining supplies limited</td>
<td></td>
</tr>
<tr>
<td>Inactivated Vero cell-derived vaccines*</td>
<td>2 doses 4 weeks apart</td>
<td>&gt; 6 months of age in endemic settings</td>
</tr>
<tr>
<td>Live attenuated vaccines (primary hamster kidney cell-derived)*</td>
<td>Single dose</td>
<td>&gt; 8 months of age</td>
</tr>
<tr>
<td>Live recombinant (chimeric) vaccines*</td>
<td>Single dose</td>
<td>&gt; 9 months of age</td>
</tr>
</tbody>
</table>

* WHO prequalified

Although all current JE vaccines are derived from genotype III strains, they elicit protective levels of neutralizing antibodies against heterologous strains of other genotypes.

Disease burden

The JE virus is the most important cause of viral encephalitis in many Asian countries, the number of estimated clinical cases being 68 000 every year. The transmission of JEV is endemic in 24 countries in the WHO South-East Asia and Western Pacific regions, which means that more than 3 billion people are exposed to the risk of infection.

The annual incidence of clinical disease varies both across and within endemic countries, ranging from <1 to >10 or higher per 100 000 population during outbreaks. The virus primarily affects children as most adults in endemic countries develop natural immunity after childhood infection. However, individuals of any age may be affected.
Annex 2: Case investigation form

<table>
<thead>
<tr>
<th>Case Identification Number: JE-_________ / __________ / __________ / __ / ______</th>
</tr>
</thead>
<tbody>
<tr>
<td>Country code/ Province code/District code/ Year/ Serial number</td>
</tr>
</tbody>
</table>

**Patient information**

<table>
<thead>
<tr>
<th>Name of health facility</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient’s name</td>
<td>Age in years / months</td>
</tr>
<tr>
<td>Date of birth dd/mm/yyyy</td>
<td>Sex Male Female Unknown</td>
</tr>
<tr>
<td>Residential address House no. Village/ town/ city: Street name: District/ province: Country: Pin/ zip code:</td>
<td>Contact number (mobile)</td>
</tr>
</tbody>
</table>

**Clinical history**

<table>
<thead>
<tr>
<th>Date of notification to public health system dd/mm/yyyy</th>
<th>Date of investigation dd/mm/yyyy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of onset of first symptom dd/mm/yyyy</td>
<td></td>
</tr>
<tr>
<td>Fever: acute onset Yes No Unknown</td>
<td></td>
</tr>
<tr>
<td>Altered mental status Yes No Unknown</td>
<td></td>
</tr>
<tr>
<td>Seizures Yes No Unknown</td>
<td></td>
</tr>
</tbody>
</table>

**Vaccination history**

<table>
<thead>
<tr>
<th>JE vaccine (type)</th>
<th>Number of doses received 1 □ 2 □ Unknown Others □</th>
<th>Date of first dose dd/mm/yyyy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of second dose dd/mm/yyyy</td>
<td>Date of other doses dd/mm/yyyy</td>
<td>Comments</td>
</tr>
</tbody>
</table>

**Investigations done**

<table>
<thead>
<tr>
<th>Type of specimen collected CSF Serum Autopsy</th>
<th>Type(s) of testing methodology IgM PRNT PCR</th>
<th>Virus isolation Others (describe)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date of collection of specimen dd/mm/yyyy</td>
<td>Number of specimen(s) collected One Two</td>
<td>Date of collection of second sample dd/mm/yyyy</td>
</tr>
</tbody>
</table>
### Laboratory results

<table>
<thead>
<tr>
<th>Dates of receipt of specimen(s)</th>
<th>dd/mm/yyyy</th>
<th>Dates of testing of specimens</th>
<th>dd/mm/yyyy</th>
<th>Date(s) of reporting of results</th>
<th>dd/mm/yyyy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Date(s) of reporting of results</td>
<td>dd/mm/yyyy</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Laboratory results for each specimen</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Classification of case

<table>
<thead>
<tr>
<th>Final classification</th>
<th>Laboratory-confirmed</th>
<th>Epidemiologically linked</th>
<th>Compatible</th>
<th>AES unknown</th>
<th>AES other agent</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Outcome

<table>
<thead>
<tr>
<th>Follow-up</th>
<th>Death</th>
<th>Survived</th>
<th>Lost to follow-up</th>
<th>Date of death/discharge</th>
<th>dd/mm/yyyy</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Comments

Investigator’s name:
Designation:
Institution:
Telephone (mobile):
Email:
Date:
Signature:
JAPANESE ENCEPHALITIS

Further reading


CONTRIBUTION

The document was produced under the strategic guidance of the Regional Director, Dr. Poonam Khetrapal Singh; Director, Programme Management Dr. Pem Namgyal, and Director CDS Dr. Suman Rijal WHO SEARO.

The entire process was overseen by Dr. Sunil Bahl, Coordinator, COVAX, Immunization and Vaccines Development.

Dr. Sudhir Khanal, IVD/CDS WHO SEARO, lead the coordination and development of the technical document together with Dr. Sudhir Joshi, IVD/CDS WHO SEARO. WHO Consultant Dr. Lalit Kant played a crucial role in updating the technical content of the document.

This document also benefited from the expert input of all the participants of the Regional workshop to review progress towards measles-rubella and other priority VPD surveillance and outbreak preparedness and response in WHO South-East Asia Region from 13-16 June 2022 in Dhaka, which included National EPI Programme Managers and VPD Surveillance Officers from Member States, as well as a number of WHO country office staff, UNICEF, and other external collaborators.

WHO HQ staff: Dr. Anindya Bose and Dr. Heidi Soeters reviewed the draft surveillance standard document and provided technical inputs.

WHO-SEARO: Dr. Jayantha Liyanage, Dr. Sigrun Roesel, Dr. Emmanuel Njambe, Dr. Lucky Sangal, Dr. Pankaj Bhatnagar, Ms. Uttara Aggarwal, Mr. Sharifuzzaman, Dr. Rajendra Bohara, Dr. Ariful Islam, Dr. Tanbir Islam, Dr. Subramanya Balakuntlam Pattabhiramaiah, Dr. Ratnesh Murugan, Dr. Stephen Chacko, Dr. Paba Palihawadana, Dr. Aishath Thimna Latheef, Dr. Balwinder Chawla, Dr. Khaing Khaing Gyi, Dr. Vinod Bura, Dr. Rahul Pradhan, Dr. Pasang Rai, Dr. Preshila Samaraweera, Ms Aree Mounsookjareoun, Dr. Sudath Peiries

UNICEF: Christopher Gregory provided inputs as well as coordinated inputs from UNICEF team to the various sections of the document.

US CDC: Dr. Ahmed Kassem, Dr. Michelle Morales provided inputs to the various sections of the document and coordinated inputs from various teams within US CDC.