

Japanese encephalitis surveillance standards*

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Complete document available online:

<http://www.who.int/vaccines-documents/DocsPDF06/843.pdf>

Japanese encephalitis

FIELD TEST VERSION

Rationale for surveillance

Japanese encephalitis (JE) is a mosquito-borne viral encephalitis that occurs in temperate and tropical regions of Asia and is maintained in a cycle of virus transmission between vertebrate amplifying hosts (e.g. pigs, herons, egrets) and several *Culex* mosquito species. The greatest transmission to humans occurs in rural settings, particularly those in which agricultural practices increase the potential for breeding of vectors or infection of vertebrate hosts. In urban settings, the potential for an outbreak of JE is low, although transmission can occur. In recent decades, JE outbreaks have occurred in areas previously non-endemic for the disease. The high case fatality rate (20%–30%) and frequent residual neuropsychiatric damage in survivors (50%–70%) make JE a major public health problem.

JE is the leading form of viral encephalitis in Asia, where about 50 000 cases and 10 000 deaths are reported each year, mostly among children. However, officially reported cases of JE greatly under-represent the true impact, due to incomplete surveillance in many affected areas. Among the control strategies, human vaccination has proven to be the single most effective control measure.

Infection with Japanese encephalitis virus may be asymptomatic, or may cause febrile illness, meningitis, myelitis or encephalitis. Encephalitis is the most commonly recognized presentation, and is clinically indistinguishable from other causes of an acute encephalitis syndrome (AES). Syndromic surveillance therefore aims to identify patients with AES, and among these confirm JEV infection using standardized laboratory techniques.

In most Asian countries, the epidemiology and public health burden of JE is poorly understood. The primary goal of disease surveillance in these countries is to characterize the epidemiology and burden of JE so as to advocate for and guide programmatic interventions.

Where JE immunization is already ongoing, the primary purpose of surveillance is to identify high-risk populations or geographic areas in need of improved vaccination coverage and areas with new disease transmission, and to document the impact of control measures.

In summary, JE surveillance is critical to characterize the epidemiology and burden of the disease, identify high risk areas for appropriate public health response and document the impact of control measures.

Japanese encephalitis (continued)

Recommended case definition

Clinical case definition

Clinically, a case of acute encephalitis syndrome is defined as a person of any age, at any time of year with the acute onset of fever and a change in mental status (including symptoms such as confusion, disorientation, coma, or inability to talk) AND/OR new onset of seizures (excluding simple febrile seizures¹). Other early clinical findings may include an increase in irritability, somnolence or abnormal behaviour greater than that seen with usual febrile illness.

Case classification

Suspected case: A case that meets the clinical case definition for AES. Suspected cases should be classified in one of the following four ways (see Figure 1).

Laboratory-confirmed JE: A suspected case that has been laboratory-confirmed as JE.

Probable JE: A suspected case that occurs in close geographic and temporal relationship to a laboratory-confirmed case of JE, in the context of an outbreak.

“Acute encephalitis syndrome” – other agent: A suspected case in which diagnostic testing is performed and an etiological agent other than JE virus is identified.

“Acute encephalitis syndrome” – unknown: A suspected case in which no diagnostic testing is performed or in which testing was performed but no etiological agent was identified or in which the test results were indeterminate.

Laboratory criteria for confirmation

Clinical signs of JE are indistinguishable from other causes of AES. Laboratory confirmation is therefore essential for accurate diagnosis of JE.

Laboratory confirmation of a JE virus infection includes:

1. presence of JE virus-specific IgM antibody in a single sample of cerebrospinal fluid (CSF) or serum,² as detected by an IgM-capture ELISA specifically for JE virus;³
or any of the following:
2. detection of JE virus antigens in tissue by immunohistochemistry; OR

¹ A simple febrile seizure is defined as a seizure that occurs in a child aged 6 months to less than 6 years old, whose only finding is fever and a single generalized convulsion lasting less than 15 minutes, and who recovers consciousness within 60 minutes of the seizure.

² A serum sample should be obtained at admission. Because it may not yet be positive in a JE-infected person, a second serum sample should be collected at discharge or on the 10th day of illness onset or at the time of death and tested for presence of JE virus specific IgM.

³ Further confirmatory tests (e.g. looking for cross-reactivity with other flaviviruses circulating in the geographical area) should be carried out: (a) when there is an ongoing dengue or other flavivirus outbreak; (b) when vaccination coverage is very high; or (c) in cases in areas where there are no epidemiological and entomological data supportive of JE transmission.

Japanese encephalitis (continued)

Recommended case definition (continued)

3. detection of JE virus genome in serum, plasma, blood, CSF,⁴ or tissue by reverse transcriptase polymerase chain reaction (PCR) or an equally sensitive and specific nucleic acid amplification test; OR
4. isolation of JE virus in serum, plasma, blood, CSF,⁴ or tissue; OR
5. detection of a four-fold or greater rise in JE virus-specific antibody as measured by haemagglutination inhibition (HI) or plaque reduction neutralization assay (PRNT) in serum collected during the acute and convalescent phase of illness. The two specimens for IgG should be collected at least 14 days apart. The IgG test should be performed in parallel with other confirmatory tests to eliminate the possibility of cross-reactivity, as indicated in footnote 3.

Note:

- The large majority of JE infections are asymptomatic. Therefore, in areas that are highly endemic for JE, it is possible to have AES due to a cause other than JE virus and have JE virus-specific IgM antibody present in serum. To avoid implicating asymptomatic JE as the cause of other AES illnesses, sterile collection and testing of a CSF sample from all persons with AES are recommended when feasible.
- Only the first 5–10 JE cases of an outbreak need be confirmed through laboratory testing. During periods of epidemic transmission of JE virus, laboratory confirmation of every case may not be necessary.

Recommended types of surveillance

JE surveillance should be conducted year round. Where feasible, surveillance for and reporting of JE should be performed within the context of integrated disease surveillance, and linked synergistically with similar surveillance activities, such as those for acute flaccid paralysis (AFP) or meningitis.

In all Asian countries

Comprehensive syndromic surveillance for acute encephalitis syndrome with aggregate reporting is recommended. In sentinel hospitals, surveillance should be case-based with specimens collected for laboratory confirmation.⁵ The number of sentinel hospitals can be gradually increased if feasible logistically.

⁴ Detection of virus genome or virus isolation in serum, plasma or blood is very specific for JE diagnosis; however, it is not sensitive as virus levels are usually undetectable in a clinically ill JE case. Therefore a negative result by these methods should not be used to rule out JE in a suspected case. Similarly detection of virus genome or virus isolation in CSF is usually only found in fatal cases and therefore not very sensitive and should not be used for ruling out a diagnosis of JE.

⁵ During epidemics, laboratory testing can be limited to confirmation of the first 5–10 cases per geographic area per epidemic.

Japanese encephalitis (continued)

Recommended types of surveillance (continued)

In Asian countries where a high level of JE control has been achieved

Surveillance should be case-based throughout the country and include laboratory confirmation of all suspect cases.

Regardless of the type of surveillance, reporting should be weekly or monthly and include “zero-reporting” (i.e. no blanks should be left in the reporting forms, a zero should be indicated when there are no cases detected). Outbreak investigations should be initiated if there is a sudden increase in cases or if cases reported are different from historical information, in terms of season, geographical area, age group, or case fatality.

Recommended minimum data elements

Aggregated data

The recommended elements for aggregated data are:

- number of cases and deaths by week/month
- number of cases by age group, sex and immunization status
- number of cases by state/province.

Case-based data

The recommended elements for case-based data are:

- unique identifier
- age
- sex
- geographical area
- travel history over the past two weeks
- whether ever immunized against JE; 1 = yes; 2 = no; 9 = unknown
- If yes, number of doses administered
- if yes, type of JE vaccine (most recently received)
- date of last JE immunization
- date of onset of first symptoms
- fever: 1 = yes; 2 = no; 9 = unknown
- change in mental status; 1 = yes; 2 = no; 9 = unknown
- seizure: 1 = yes; 2 = no; 9 = unknown
- date CSF sample taken
- date serum sample 1 taken
- date serum sample 2 taken
- autopsy specimen taken: 1 = yes; 2 = no; 9 = unknown
- clinical diagnosis: _____

Japanese encephalitis (continued)

Recommended minimum data elements (continued)

Depending on which laboratory tests used for serum or CSF:

- IgM serum 1 results: 1 = positive; 2 = negative; 3 = not tested; 9 = unknown
- IgM serum 2 results: 1 = positive; 2 = negative; 3 = not tested; 9 = unknown
- IgM CSF results: 1 = positive; 2 = negative; 3 = not tested; 9 = unknown
- virus detection (PCR, virus isolation, immunohistochemistry) results: 1 = positive; 2 = negative; 3 = not tested; 9 = unknown
- HI or PRNT results on acute and convalescent sera: 1 = positive (4 fold rise or greater); 2 = negative (<4 fold rise); 3 = not tested; 9 = unknown
- date serum 1 results reported
- date serum 2 results reported
- date CSF results reported
- date virus detection results reported
- final classification: 1= laboratory confirmed JE; 2= probable JE; 3 = AES unknown; 4 = AES other agent
- status at discharge: 1 = alive; 2 = dead; 9 = unknown
- date of death or discharge.

Recommended data analyses, presentations, reports

Aggregated data

The recommended elements for aggregated data are:

- number and incidence of suspected cases by week, month, year, age group, and geographic area;
 - number and incidence of confirmed cases by week, month, year, age group, and geographic area;
 - JE vaccine coverage by year and geographical area;
 - percentage of cases vaccinated and unvaccinated; and
- completeness/timeliness of monthly reporting by geographical area.

Case-based data

The recommended elements for case-based data are the same as those for aggregated data plus the following:

- suspected and confirmed cases – age-specific, gender-specific, geographic area-specific, and immunization status-specific incidence;
- percentage of suspected cases with CSF and/or serum specimens;
- percentage of cases with serum 10 or more days after onset of illness (when testing methodology is IgM-capture ELISA);
- case fatality ratio;
- final classification of all suspect cases; and
- proportion of AES attributed to JE.

Japanese encephalitis (continued)

Recommended data analyses, presentations, reports (continued)

Performance indicators of surveillance quality

The following targets are for countries with a well established AES surveillance system (Table 1 and Table 2). Countries commencing with JE surveillance may set intermediate targets.

Table 1: Targets for countries with established surveillance systems

Indicator	Target
Completeness of monthly reporting	> 90%
Timeliness of monthly reporting	> 80%
Percentage of serum samples taken a minimum of 10 days after onset (When the testing methodology is IgM-capture ELISA)	> 80%

In countries where a high level of JE control has been achieved, the following indicators can be helpful as managerial tools to identify areas where corrective action is needed (Table 2).

Table 2: Indicators to assist corrective action

Indicator	Target
Percentage of all suspect cases for which specimens were collected	> 80% ^a
Percentage of CSF/serum samples reaching laboratory in adequate ^b condition	> 80%
For all tests, laboratory results reported < 1 month after receipt specimen	> 80%

^a Only applicable for countries doing nationwide case-based surveillance.
^b "Adequate condition" means the specimen is transported using reverse cold chain.

Japanese encephalitis (continued)

Principal uses of data for decision-making

The principal uses for decision-making are to:

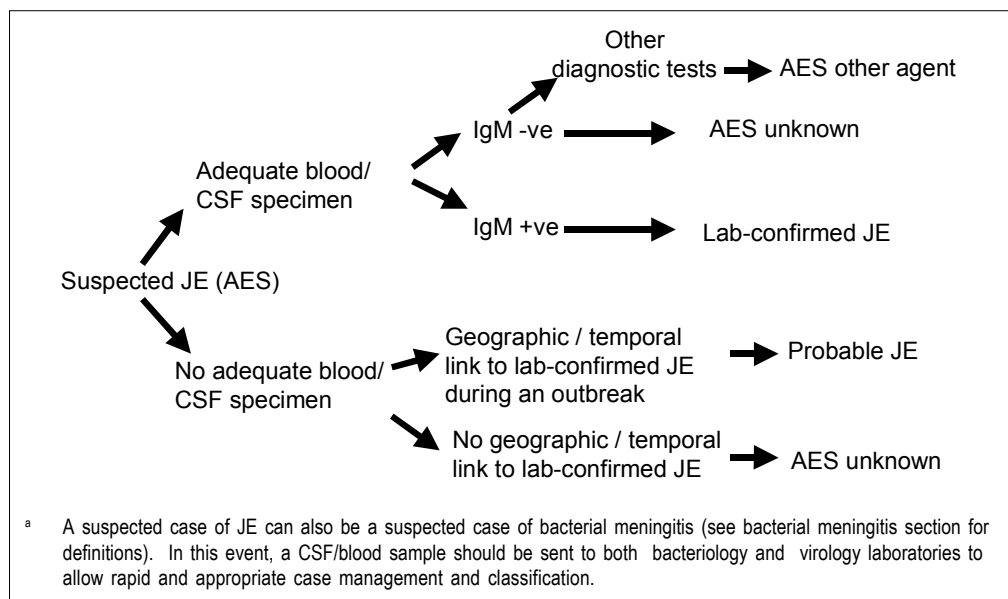
- guide policy and strategies on JE control;
- assess the impact of vaccination;
- identify geographic areas or populations at high risk to further guide where immunization coverage should be improved;
- monitor the performance of surveillance;
- monitor the performance of the laboratory; and
- monitor vaccine efficacy.

Special aspects

For persons vaccinated with Japanese encephalitis vaccine within six months of illness onset, testing a single serum sample for Japanese encephalitis IgM may not be diagnostic because it may give a false positive result. In such cases, a diagnosis can only be confirmed by demonstrating JE IgM in the CSF, JE virus isolation, a positive nucleic acid amplification test, immunohistochemistry, or a four-fold or greater rise in antibody titre in acute and convalescent phase serum samples.

Efforts should be made to identify other causes of AES. As a general rule, persons with acute encephalitis should undergo a lumbar puncture to obtain CSF to identify other treatable agents that may result in an illness that manifests as acute encephalitis syndrome. CSF with WBC = 1000/mm³ is unlikely to be due to Japanese encephalitis or any other arbovirus; in these cases, bacterial causes of purulent meningitis such as *Haemophilus influenzae*, *Neisseria meningitidis*, or *Streptococcus pneumoniae* should be considered. In malaria-transmission areas, malaria testing should be carried out to rule out cerebral malaria. Health care providers should also rule out herpes encephalitis, if possible, as it is a treatable cause of AES.

Figure 1: Final classification scheme for AES cases ^a



^a A suspected case of JE can also be a suspected case of bacterial meningitis (see bacterial meningitis section for definitions). In this event, a CSF/blood sample should be sent to both bacteriology and virology laboratories to allow rapid and appropriate case management and classification.