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Background information

Introduction

Japanese encephalitis (JE) occurs in Asia and is the most important cause of viral encephalitis in the world.\(^1\) With the decrease in polio, JE is now the leading cause of viral neurologic disease in Asia. Children between the ages of 1 to 15 years are most commonly affected; however, adults too can be infected in populations where the virus is newly introduced to the area.\(^4\) Over 50,000 cases are reported annually with 10,000 to 15,000 deaths. This figure is believed to represent only a small proportion of the disease burden that actually exists.\(^6\) Approximately 3 billion people live in areas at-risk for JE with 700 million children in the highest risk age group (<15 years).\(^6,8\) Diagnostics for JE are not widely available in poor rural areas where the disease is endemic, making accurate surveillance and reporting difficult. Present incidence rates vary significantly from 1.8 to 64 per 10,000.\(^6\) Using a modest incidence rate of 2.5 per 10,000, without immunization, an estimate of 175,000 cases would be expected annually.\(^6\) This figure shows the potential magnitude of underreporting that may occur with JE. Fatality rates also vary but on average approximately 30 percent of JE patients die. For those that survive a JE infection about half to three quarters will have a JE-related disability including intellectual, behavioral, and neurological sequelae.

About the virus

Japanese encephalitis is caused by an arbovirus in the Flaviviridae family similar to West Nile, Murray Valley, and St. Louis encephalitis. It is a single-stranded RNA virus transmitted by a mosquito vector, most commonly the species *Culex tritaeniorhynchus*. *C. tritaeniorhynchus* mosquitoes lay their eggs in quiet pools such as rice paddy fields or drainage ditches. The pig is found to be the primary amplifying host of the virus, displaying very high levels of viremia. JE has no overt signs of illness in pigs but is associated with higher rates of spontaneous abortion and stillbirths when the infection occurs during pregnancy. Birds, such as herons or ducks, have also been implicated in the transmission of JE. Cattle and buffalo, although infected with JE, have low levels of viremia and are not believed to play a roll in transmission.

Clinical picture

The incubation period for JE ranges from 4 to 14 days. The clinical picture of infection has four stages: prodromal, acute, subacute, and convalescent. The prodromal stage lasts from 2 to 3 days and has a high fever with severe headache. Nonspecific symptoms include malaise, anorexia, nausea, and vomiting.

In the acute phase, lasting 3 to 4 days, the patient develops a change in the state of consciousness, which can range from mild clouding to stupor and coma. It is during this phase that patients frequently present for health care. Seizures are common and the patient
remains febrile with weakness and stiff neck frequently seen. Less commonly observed are tremor, abnormal movements, and cranial nerve involvement. Fatal cases usually deteriorate rapidly at this stage and die.\textsuperscript{6,9}

The subacute phase lasts 7 to 10 days and in uncomplicated cases the fever decreases over a period of 1 to 2 weeks and neurological sequelae may improve. In severe cases, secondary infections are common during this phase including bladder infections, pneumonia, and bedsores. Close attention by caregivers can minimize these problems.

During the convalescence phase, mild cases may recover completely over the next several weeks. Severe cases may improve somewhat but are frequently left with neurological sequelae. Late developing sequelae have also been described such as optic nerve degeneration and seizures.\textsuperscript{10}

The clinical presentation of JE cannot accurately be differentiated from other etiologies of meningioencephalitis and requires laboratory diagnostic confirmation. Interestingly, in Vietnam 55\% of patients identified with acute flaccid paralysis (AFP) were actually later diagnosed with JE.\textsuperscript{11}

Disability

Disability and sequelae have been found in 40\% to 75\% of surviving JE patients. Disability determinations vary depending on the type of sequelae included in the study and the timing of the follow up.\textsuperscript{6,10} Sequelae fit into four major categories: motor, behavior, intellectual, and other neurologic.\textsuperscript{12} Motor deficits are common in approximately 30\% of survivors, with significant cognitive and language impairments in 20\%. A direct relationship exists between the percentage of survivors and the amount and severity of sequelae (i.e., the more people survive the more people are left with disabilities).\textsuperscript{13} There is also evidence to show that sequelae can develop as well as resolve over time.\textsuperscript{10,14} From a study in Thailand, fine motor disability, aggressiveness, uncontrolled emotion/impulsiveness, and abnormal intelligence were the most common sequelae occurring in greater than 70\% of patients.\textsuperscript{12} JE is also associated with seizures and Parkinson’s disease.\textsuperscript{10,15}

Diagnosis

Japanese encephalitis infections are asymptomatic in a majority of people infected with the JE virus. The ratio of asymptomatic infections for every JE case ranges from 50:1 to 300:1. Therefore, in order to confirm a case of JE a patient must have clinical evidence of JE infection in addition to positive serology.\textsuperscript{16} Identification of JE immunoglobulin M (IgM) in cerebral spinal fluid (CSF) indicates the presence of JE virus in the central nervous system (CNS). A definitive diagnosis of JE can be made with viral isolation from CSF or, in fatal cases, CNS tissue; but viral isolation is not possible in most cases due to low titers and rapid neutralizing antibody.\textsuperscript{2,17} The standard of JE diagnosis in practice is IgM-capture enzyme-linked immunosorbent assay (ELISA). Seventy-five percent of CSF and serum samples will be IgM positive at four days after onset of fever, but almost all samples drawn one week after
presentation will be positive. The CSF will usually have a pattern that is consistent with a viral infection—slightly elevated protein, normal glucose, and lymphocyte pleocytosis. CSF is desired for diagnosis as it confirms a CNS infection and has higher titers than serum; however, a single serum specimen in a patient with a clinical syndrome consistent with encephalitis can be diagnostic. Paired sera tested for total antibody can also be used for diagnosis looking for a four-fold rise in titer between acute serum, drawn at presentation, and convalescent serum, usually drawn two weeks after the acute serum. Difficulty in diagnosis arises in areas where several flaviviruses coexist. There is significant cross-reactivity among flaviviruses, particularly immunoglobulin G (IgG), so that a dengue and West Nile infection can give a small increase in JE titers and vice versa. It may be necessary to test for dengue and West Nile in areas where these viruses co-circulate.

Other diagnostic tests are available but are slowly being replaced by the ELISA: hemagglutination inhibition tests (HI) are not as sensitive or specific as IgM capture ELISA and have cross-reactivity with other flaviviruses, plaque reduction neutralization tests (PRNT) are time consuming and difficult to perform, and a polymerase chain reaction is primarily only in use for research purposes. The international community has recognized a need for simplified diagnostics for accurate decentralized diagnosis; these tools could help improve the detection of JE and improve disease burden data. Three new JE IgM antibody capture ELISAs have been developed, and two are now commercially available. Field testing of the kits for sensitivity, specificity, and usability is being conducted. A dot-blot assay has been developed and tested in the field, which is incubated at room temperature and then overnight at 4°C. This test compared to the IgM ELISA has a 83% sensitivity and 99% specificity. The sensitivity increases to 98% when both CSF and serum are tested. In addition, a dipstick and an immunofluorescin slide test are being developed for use in diagnosis of arboviruses including JE, which also require minimal equipment and training, but are not commercially available. If these tools could be used on a broader scale the true incidence of disease could be easier to determine and data could be generated to improve control programs and initiate vaccination where appropriate. One possible solution to this problem is the use of desiccated blood specimens that can be easily transported to a referral lab.

**Treatment**

There is no specific therapy for Japanese encephalitis. Care of JE patients is focused on supportive care. JE requires attentive care through the acute and convalescent phases and careful attention to early rehabilitation. By providing diligent care, the case fatality rates can be greatly reduced. In India, in a retrospective study of 12,506 cases, the top causes of death were aspiration, hypoxia, hypoglycemia, and uncontrolled seizures. Supportive care, therefore, should focus on airway management, seizure control, decreasing cerebral edema, fluids and nutrition, fever control, and managing secondary infections.

**Distribution**

JE is widespread across Asia and has continued to spread over the past 25 years. Some countries affected by JE include China, India, Nepal, Sri Lanka, Thailand, Vietnam,
Laos, Cambodia, Indonesia, Malaysia, Japan, Myanmar, Philippines, South Korea, Russian Federation, and islands in the Torres Strait, Australia. Human behavior and agricultural practices, especially rice paddy cultivation are thought to have impacted JE transmission and distribution.25

Control programs

Control programs for JE have been focused in three major areas: mosquito control, amplifying host (pig) control, and vaccination. However, neither mosquito control nor amplifying host (pig) control have been proven to be effective public health measures to control disease.6,13,32

Mosquito control can include spraying, draining mosquito habitats, and the use of bednets. Such spraying is both resource intensive and expensive. While spraying is important in the control of many vector-borne diseases, it is frequently ineffective in the control of JE.4 To be effective these control measures must cover all mosquito habitats, which include rice paddy fields, puddles, and drainage areas. This is difficult anytime, but especially difficult in monsoon season and in rural rice growing areas where JE is most common. The time it takes a *Culex* mosquito to develop from an egg to an adult is 10 to 12 days. Therefore, in addition to the large area to be included in control programs, spraying must also be repeated very frequently (every 10 to 12 days) to control mosquito populations.33

Bednets have not been shown to be effective. The reason may be that the *Culex* mosquito bites in the twilight hours and only young children that are in bed in the early evening would receive benefit from their use. The at-risk population for Japanese encephalitis is 1 to 15 years of age so a large portion of the at-risk population will still be exposed despite the use of bednets.21 Bednets may be important for the control of many vector-borne diseases besides JE and should be continued although alone cannot be relied on to control JE.4

As the vector of JE is hard to control, additional efforts have been directed to the main amplifying host, the pig. Pig control has been attempted in three ways: segregation, slaughtering, or vaccination. Pigs must be segregated and contained at least 5 km from humans (the flying radius of the mosquito vector), which is not practical in most developing world settings. Slaughtering has a high economic impact and affects many families ability to make a living. Pig vaccination has not been shown to significantly impact human cases of JE and is costly, difficult, and very time consuming.6,34

In Singapore the urbanization of the entire country has stopped viral transmission; however, this model is not realistically reproducible.6 A recent evaluation of JE in Thailand has described the development of their JE control program from use of environmental control measures for outbreak control to the initiation of their vaccination program.35 From 1973 until 1983, a vertical control program with vector control, case detection, and outbreak response was used without much effect on disease burden; in 1983 this program was integrated into the primary health care system as a horizontal control program which also had little effect.35 However, when JE vaccine was introduced into the country the incidence of JE fell dramatically.
Vaccination of humans is the only realistic tool to control JE.\textsuperscript{6,18,32} Vaccination has been used to control JE in Japan, South Korea, Taiwan, China, and Thailand.\textsuperscript{6,32} The US Centers for Disease Control and Prevention Workgroup of Viral Disease stated “the key to controlling JE is to incorporate the vaccine into EPI programmes in Asia”.\textsuperscript{36} In addition, the World Health Organization (WHO) has recommended the use of vaccine for JE control where the vaccine is affordable.\textsuperscript{5,6,37}

**JE vaccine**

There are now three JE vaccines used worldwide: inactivated mouse brain-derived vaccine, inactivated primary hamster kidney cell-derived vaccine, and live attenuated SA 14-14-2 vaccine. No JE vaccines are currently prequalified, although it is anticipated the SA 14-14-2 vaccine will be submitted for prequalification in early 2007.

The most widely available JE vaccine internationally has been the inactivated mouse brain-derived vaccine using either the Nakayama or Beijing JE strains. The vaccine is available commercially from producers in Japan and Korea and is produced by governments in India, Taiwan, Thailand, and Vietnam. However, some manufacturers have recently ceased production of this vaccine and supply is insufficient for demand.

One- to two-year protection of a two-dose regimen has shown 80\% to 91\% efficacy.\textsuperscript{4} Three doses are needed in populations without previous exposure to flaviviruses.\textsuperscript{4,6} The vaccine schedule generally recommended is two doses given one month apart and the third dose one year later with boosters at three-year intervals.\textsuperscript{4} However, in practice, the use of the vaccine varies widely from country to country with the first doses separated by as little as one week and the boosters given more frequently.\textsuperscript{38} Since the early 1990s concerns over the safety of the vaccine have arisen. Hypersensitivity reactions have been described in 0.5\% of recipients.\textsuperscript{36} Several of these reactions had a delayed onset with a median of 12 hours from the first dose and 3 days from the second dose.\textsuperscript{4} In 1994, several severe systemic reactions were seen in Korea temporally related to the vaccine.\textsuperscript{38,39} Neurological complications including acute disseminated encephalomyelitis have been reported in Japan, Denmark, and Korea.\textsuperscript{38}

The SA 14-14-2 vaccine is made from a neuroattenuated viral strain that has shown effectiveness in a lab setting against the P3; Nakayama; 12 Chinese JE field isolates; and JE strains from Thailand, Nepal, Vietnam, Indonesia, India, Japan, and Philippines. This vaccine has been licensed in China since 1988 and over 200 million doses have been given. The vaccine has a 96\% to 98\% efficacy in China.\textsuperscript{40-42} A study recently completed in Nepal reported a 98.5\% efficacy 12 to 15 months after immunization with a single dose of vaccine.\textsuperscript{43} Single-dose use is consistent with studies done in China that show the protection of a single dose of SA 14-14-2 in animal studies.\textsuperscript{40} Studies in China have shown protective efficacy up to 12 years after a 2 shot regimen.\textsuperscript{40} The present recommendations in China are for two doses given one year apart followed by a booster at six years; however, a single dose schedule appears feasible.\textsuperscript{1} The safety of the vaccine has been studied multiple times in greater than 600,000 children 1 to 15 years of age. Fever occurred in less than 1 per 500, and
there were no associated encephalitis cases.\textsuperscript{6,40} In one study of 25,000 children who were closely followed, the vaccinated group showed no difference in symptoms compared to the control group.\textsuperscript{1,6} This vaccine is also produced inexpensively in China.

South Korea, Nepal, and Sri Lanka have all licensed this vaccine for use. Prior to 2000, concerns over the cell line used for production (primary hamster kidney cells) had also been an issue for international use of the vaccine, but WHO has now provided guidelines for quality control that address this issue.\textsuperscript{44}

The inactivated primary hamster kidney cell vaccine is used exclusively in China. It is made from the P3 strain which is similar to the Beijing strain and has broad heterologous immunity. Although the vaccine is inexpensive to produce, the low efficacy and frequent boosters have resulted in decreased use, and this vaccine is slowly being replaced by the more efficacious live, attenuated SA 14-14-2 vaccine.

Several new vaccines are in development.\textsuperscript{45-47} A new chimeric vaccine is undergoing clinical trials and looks promising (Table 1). An inactivated vero cell-derived vaccine is also in development.

\textbf{Table 1. Summary of JE vaccines currently available or in development.}

<table>
<thead>
<tr>
<th>JE Virus Vaccine</th>
<th>Derivation</th>
<th>Estimated Efficacy (percent)</th>
<th>Locations vaccine in use</th>
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<tr>
<td>Inactivated</td>
<td>Mouse brain tissue</td>
<td>80 to 91</td>
<td>Japan, Korea, Thailand, Sri Lanka, Vietnam, certain states of India.</td>
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<tr>
<td>Live, attenuated (SA14-14-2 strain)</td>
<td>Primary hamster kidney cell</td>
<td>96 to 100</td>
<td>China, Korea, Nepal</td>
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<tr>
<td>Inactivated</td>
<td>Primary hamster kidney cell</td>
<td>76 to 95</td>
<td>China</td>
</tr>
<tr>
<td>Chimeric, live</td>
<td>Yellow fever/JE virus (Y17D/SA14-14-2) chimeric</td>
<td>Undergoing clinical trials</td>
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<tr>
<td>Inactivated</td>
<td>Vero cells</td>
<td>Undergoing clinical trials</td>
<td>Undergoing clinical trials</td>
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\textbf{Disease burden estimates}

The disease burden of JE is still not well-defined (Table 2). WHO encourages reporting but it is incomplete and in many cases not likely to be accurate. Diagnostic confirmation of cases
occurs infrequently and is not available at all in several parts of the world. Therefore, some countries do not diagnose JE at all, and it is believed not to be a problem. Other countries report all clinically suspected encephalitis cases and may actually overestimate the cases of JE.

Table 2. JE disease burden in WHO South East Asia (1999 to 2004) and Western Pacific regions (1995 to 2000).

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Sentinel surveillance for Japanese encephalitis

Aim

To define the disease burden from JE in at-risk countries and provide data to enable planning for disease control measures.

Objectives

1. To determine the percent of viral encephalitis patients admitted to the hospital with lab–confirmed JE disease.
2. To determine the mortality and morbidity from Acute Encephalitis Syndrome (AES) and JE.
3. To determine the geographic and age distribution of AES and JE patients.
4. To determine the distribution of AES and JE over time and season.
5. To determine the case fatality rates of JE and other AES cases.

Design

Commonly, surveillance for AES is carried out on a nationwide basis. Encephalitis due to JE virus cannot be distinguished clinically from encephalitis due to other causes, so laboratory testing is required to confirm cases. In some settings (e.g., in countries in which an immunization program has been implemented), case-based surveillance for JE is recommended. This means every case of encephalitis is tested to determine if it is due to JE virus, so outbreaks can be detected or areas where intervention is necessary can be determined. In other places, immunization has not been implemented widely and disease burden from JE is still high. Sentinel site surveillance can be used effectively in such settings, to determine and define disease burden.

Sentinel site surveillance refers to particular hospitals being chosen as sites where more intensive surveillance and testing for JE is undertaken. JE is a severe clinical illness that will most commonly be cared for in a hospital setting. Therefore, hospital based surveillance is the most effective means of surveillance for this disease. The proportion of all AES cases that are due to JE can be determined at sentinel sites. This data can be extrapolated to determine the national disease burden from JE and other information on AES.

The design of surveillance and collection of data from sentinel sites can be modified to account for several different levels of health care infrastructure. These could fall in three basic areas:

1. Level A
   a. Hospitals where CSF is routinely drawn on patients presenting with meningitis or encephalitis.
   b. Diagnostic laboratory has ELISA testing capability.
2. Level B
   a. Hospitals where CSF may or may not routinely be drawn on patients presenting with meningitis or encephalitis.
   b. No diagnostic laboratory with ELISA diagnostics in the facility but testing is available at a known referral laboratory.
   c. Good cold chain capability and transportation to referral laboratory is possible.

3. Level C
   a. Hospitals or treatment centers where CSF is not routinely drawn on patients and no qualified staff is present. Blood may or may not be routinely used in patient work up.
   b. No diagnostic laboratory with ELISA diagnostic capability in the area.

**Hospital selection**

The hospitals selected should be selected after considering key sites for inclusion and after a feasibility trip to assess referral patterns and history in the at-risk area. Key sites may include those that are in particular geographical areas and/or those in areas known to have high disease burden. Capacity for testing, as described above, should also be considered. For example, the first hospital could be a tertiary care hospital in the capital that will receive patients with a neurological illness or neurological complications that would be referred from rural sites to the capital. JE is a rural disease associated with rice paddy cultivation with pigs as the primary amplifying host, therefore, as other possible surveillance sites, provincial or district hospitals in high-risk regions may be desirable depending on the size of the catchment population and referral patterns.

**Hospital site feasibility assessment**

Before choosing sites for inclusion, it is suggested a feasibility assessment is undertaken, by visiting each sentinel site that may possibly be included. The following procedure is suggested:

1. Review medical records at the selected hospital to confirm that patients with the desired case definitions are seen at that hospital. If not, assess where a patient with the case definition would be cared for and consider that hospital as a site. Determine where the patient will initially present and where they will be cared for to include all health care practitioners who may care for the patient in training and information sharing.

2. Determine the routine work up of a patient presenting with meningitis or encephalitis symptoms (i.e., which specimens are collected, which tests are done) Make note of all the diagnostics routinely performed and whether they are performed in the hospital or at a referral lab. Possible scenarios include:
   a. Patients with the case definition have laboratory specimens, either CSF and/or serum, collected and tested as part of their work up. Then: Facility is OK as a surveillance site.
b. Patients have no routine work up for this presentation but the hospital has the diagnostic capabilities to do ELISA either at the facility or a referral lab that works with the facility. Then: Facility is OK as a surveillance site but additional training will need to be provided for laboratory staff and providers involved in patient care.

c. Patients have no routine work up for this presentation and they have no diagnostic capabilities to do ELISA either at the facility or a referral lab that works with the facility. Then: consider if this is an important site for surveillance. Look at options for specimen collection (e.g., filter paper) and testing.

Methods

Case definition for surveillance

WHO has prepared standards for surveillance for Japanese Encephalitis which include a suggested case definition for surveillance purposes (http://www.who.int/vaccines-documents/DocsPDF06/843.pdf). Surveillance is based on detecting cases of AES and conducting JE laboratory testing, as possible, to determine etiology of cases. Modifications to the case definition could be considered, for example, to focus on the most heavily affected age groups or include cases of AFP.

Patient management

Cerebrospinal fluid should be drawn and analyzed on each patient that meets the case definition, where possible. The purpose of this is to identify bacterial, and thus treatable, causes of AES to enable appropriate and immediate treatment. The remaining CSF sample would be submitted for virological JE testing (JE IgM ELISA). Additionally, a serum sample should be drawn on admission and again at least seven days after admission (or before discharge or death) for JE serology (JE IgM ELISA).

*Level A* - The appropriately labeled sample should be submitted to the facility laboratory for JE IgM ELISA, and the test results reported to the provider for subsequent use in the patient’s care and reported through the surveillance system.

*Level B* - The labeled sample, after appropriate testing in the facility lab to their capabilities, should be stored at –20°C until transported with adequate cold chain to the selected referral laboratory for JE IgM ELISA. The test results should be reported to the provider for subsequent use in the patient’s care and reported by the laboratory through the surveillance system.

*Level C* - The blood sample can be obtained from a routine blood draw or from a finger or, in infants, a heel stick. The labeled blood sample, after appropriate testing in the facility lab to their capabilities, should be dried on filter paper and sent by mail or other arranged transportation with the patient’s data entry sheet record to the identified referral laboratory. The sample should be stored dry and at room temperature until testing. The test results
should be reported to the provider for subsequent use in the patients care (most likely after discharge) and through the surveillance system.

**Data management**

A surveillance form should be completed for each patient. This can be as simple or comprehensive as desired, depending on questions that need to be answered. As a minimum, it is recommended information on age, sex, date of onset, place of residence, minimal clinical history, vaccination history, and outcome should be collected (see Annex A for an example). It must be ensured surveillance information can be linked to laboratory information. For example, a unique identification number can be used on all patient data forms, the hospital record, laboratory form, and on clinical specimens submitted for JE diagnostics. On the patient’s discharge, the surveillance form should be submitted to the identified government department in charge of surveillance or special investigators for additional analysis.

**Laboratory analysis**

CSF and serum should be tested by IgM Capture ELISA.

**Monitoring and supervision**

Data should be reviewed weekly to monthly in the selected hospital, and the log of admitted patients should be compared to the emergency room log and hospital admission records to see that all patients meeting the case definition were reported. Surveillance forms should be reviewed for completion and the percentage of patients enrolled with proper specimens collected, and lab results recorded should be noted. Suggested indicators for surveillance are provided in the WHO surveillance standards. Feedback should be provided to the practitioners to improve data quality in any areas with a noted weakness.

**Reporting**

Results of surveillance should be provided to the appropriate health authorities so that proper disease control strategies can be planned and public health priorities can be established based on the available data.
Annex A: Data collection and laboratory forms

The attached forms provide examples of a surveillance and a laboratory form, based on forms originally developed by the International Vaccine Institute, Korea. These forms can be used directly or be modified to suit the site selected for surveillance. The form can be simplified or expanded according to the questions of the surveillance team. The minimum data collected should include the age of the patient, place of residence, the date of onset (or presentation), vaccination history, minimal clinical history, and condition at discharge.
Questionnaire for Acute Encephalitis Syndrome Surveillance

[1] PATIENT unique ID number: _________________________________

CLINICIAN INFORMATION:
[2] Name of hospital where patient evaluated: ________________________________
[3] Date of evaluation (DD/MM/YY): ____/____/______

CLINICAL SCREENING CRITERIA:
A case of suspected JE is defined as a patient who presents to the participating health facility and:

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>[4] Aged &gt; 1 month and ≤ 15 years</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>[5] Has acute febrile illness</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>[6] a change in mental status (such as confusion, disorientation, inability to talk, coma) or</td>
<td>☐</td>
<td>☐</td>
</tr>
<tr>
<td>[7] new onset seizures, excluding simple febrile seizures (defined as a single seizure lasting &lt; 15 minutes with recovery of consciousness within 60 minutes, in a child aged 6 months to 5 years) or</td>
<td>☐</td>
<td>☐</td>
</tr>
</tbody>
</table>

PATIENT DEMOGRAPHIC INFORMATION:
[10] Medical record number: ____________________________
[12] Has the patient traveled anywhere outside of the geographic area in the past 2 weeks? a. Y b. N
[13] If yes, where ___________________________________________________________________

CLINICAL HISTORY INFORMATION AT PRESENTATION TO HOSPITAL:
[14] Date of first symptom onset (DD/MM/YY): ____/____/______
[15] What was first symptom or sign?  
   f. Bulging Fontanel  g. Headache  h. Other (please write): __________________________
[16] Pre-Existing conditions:  
   a. None  b. Congenital condition  c. Neurocysticercosis  d. Epilepsy  e. Trauma
   f. Immune Suppression (e.g. from drugs/disease)  g. CSF Shunt  h. Other (please write)________________

Signs/symptoms since onset of illness when presenting to the hospital:  
[26] Other sign or symptom:________________________________________

HOSPITAL ADMISSION INFORMATION:  
[27] Was the patient admitted to the hospital  a. Y  b. N
[28] If no, why not ________________________________________________________________
[29] Date of admission (DD/MM/YY): ____/____/______
[30] Presumptive (working) diagnosis:  
e. Fever of Unknown Origin  
f. Febrile Seizure  
g. Other: ______________________________

**FAMILY INFORMATION:**

[31] How many people live in the patient's home (including the patient) ______

[32] Do any other family members have similar symptoms?  
   a. Y  
   b. N

**HOUSING INFORMATION:**

[33] Is rice field near your home?  
   a. Y  
   b. N  
   c. Don't know

[34] Distance to nearest rice field:  
   a. < 1 km  
   b. 1-5 km  
   c. >5 km  
   d. Don't know

[35] Does the family or neighbor own domestic animals? (More than one item may be circled):  
   a. pig  
   b. cattle  
   c. buffalo  
   d. goat  
   e. sheep  
   f. duck  
   g. chicken  
   h. others specify: ______

**JE VACCINATION HISTORY:**

[36] Has the patient been vaccinated against JE?  
   a. Y  
   b. N

[37] If yes, how many have they received? ______

[38] If yes, please provide the date of vaccination if known:  
   [39] Dose 1  
       ______/_____/_____
   [40] Dose 2  
       ______/_____/_____
   [41] Dose 3  
       ______/_____/_____

[42] What is the source of Vaccination History?  
   a. vaccination card  
   b. memory of parents  
   c. Documentation at health center  
   d. Other

**HOSPITAL COURSE INFORMATION:** New signs or symptoms after admission:

[43] Fever:  
   a. Y  
   b. N

[44] Aphasia  
   a. Y  
   b. N

[45] Headache  
   a. Y  
   b. N

[46] Focal Neurologic Sign  
   a. Y  
   b. N

[47] Seizure:  
   a. Y  
   b. N

[48] Spasticity  
   a. Y  
   b. N

[49] Mental Status↓:  
   a. Y  
   b. N

[50] Lowest Glasgow Coma Score ______

[52] Other sign or symptom including other neurologic changes: ______________________________

**Secondary Infections/complications:**

[53] Pneumonia  
   a. Y  
   b. N

[54] Urinary infection  
   a. Y  
   b. N

[55] Bed sore  
   a. Y  
   b. N

[56] Corneal ulcer  
   a. Y  
   b. N

[57] Other secondary infections/complications: ____________________________________________

**DISCHARGE INFORMATION:**

[58] Date of discharge or death (DD/MM/YY): ______/_____/_____

[59] Discharge on request?  
   a. Y  
   b. N  
   c. Don't know

[60] If Yes, reason for discharge on request:  
   a. Economic reason  
   b. No improvement in condition  
   c. Other: ________________  
   d. Don't know

[61] What was the patient's status at discharge from the hospital?  
   a. Alive, well  
   b. Alive, disabled  
   c. Alive, still sick  
   d. Dead  
   e. Don't know

[62] If the patient died, what was the cause of death? ______________________________

[63] What was clinical diagnosis at discharge? (more than one diagnosis may be circled):  
   a. Viral Encephalitis  
   b. Bacterial Meningitis  
   c. Acute Flaccid Paralysis  
   d. Aseptic Meningitis  
   e. Febrile Seizure  
   f. Epilepsy Precipitated by Fever  
   g. Gastroenteritis  
   h. Epilepsy  
   i. Dengue Fever  
   j. Tuberculous Encephalitis  
   k. Other (please write): ______________________________
Laboratory Questionnaire for Japanese Encephalitis Surveillance

PATIENT unique ID number: __________________________________________
Patient name: ______________________________________________________
Age ______
Gender:  Male  Female
Name of evaluating doctor: __________________________________________
Name of hospital where patient evaluated: ______________________________

LABORATORY INFORMATION:

<table>
<thead>
<tr>
<th>Specimen</th>
<th>CSF # 1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Specimen Number</td>
<td></td>
</tr>
<tr>
<td>Collection date and time (DD/MM/YY)</td>
<td><em><strong>/</strong></em>/___  <em><strong>/</strong></em></td>
</tr>
<tr>
<td>Testing date (DD/MM/YY)</td>
<td><em><strong>/</strong></em>/___  <em><strong>/</strong></em></td>
</tr>
<tr>
<td>CSF Glucose (mg/dL)</td>
<td></td>
</tr>
<tr>
<td>CSF Protein (mg/dL)</td>
<td></td>
</tr>
<tr>
<td>CSF Total WBC (cells/mm³)</td>
<td></td>
</tr>
<tr>
<td>Differential cell count</td>
<td></td>
</tr>
<tr>
<td>Polymorphonuclears (%)</td>
<td></td>
</tr>
<tr>
<td>Lymphocytes (%)</td>
<td></td>
</tr>
<tr>
<td>JE-Specific Enzyme Immunoassay (EIA)</td>
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</table>

**Comments on CSF:**
____________________________________________________________________________
____________________________________________________________________________

<table>
<thead>
<tr>
<th>Specimen</th>
<th>SERUM # 1</th>
<th>SERUM # 2</th>
</tr>
</thead>
<tbody>
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<td>Specimen Number</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Collection date and time (DD/MM/YY)</td>
<td><em><strong>/</strong></em>/___</td>
<td><em><strong>/</strong></em>/___</td>
</tr>
<tr>
<td>Testing date and time (DD/MM/YY)</td>
<td><em><strong>/</strong></em>/___</td>
<td><em><strong>/</strong></em>/___</td>
</tr>
<tr>
<td>Glucose (mg/dL)</td>
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<tr>
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</table>

**Comments on Serum:**
____________________________________________________________________________
____________________________________________________________________________

____________________________________________________________________________
____________________________________________________________________________
Reference List


