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## List of Abbreviations

ADEM	Acute Disseminated Encephalomyelitis
AEFI	Adverse Effects Following Immunization
AES	Acute Encephalitis Syndrome
АМОН	Additional Medical Officer of Health
CD	Communicable Diseases
CDR	Communicable Disease Report
CFR	Case Fatality Rate
CNS	Central Nervous System
CSF	Cerebro Spinal Fluid
DAPH	Department of Animal Production and Health
DPT	Diphtheria, Pertussis, Tetanus
EIA	Enzyme Immuno Assay
ELISA	Enzyme Linked Immuno Sorbent Assay
H544	Health 544 (Notification of a communicable disease)
HAI	Haemagglutination Inhibition
HI	Haemagglutination Inhibition
lgG	Immunoglobulin G
lgM	Immunoglobulin M
JE	Japanese Encephalitis
JEV	Japanese Encephalitis Virus
LJEV	Live Attenuated Japanese Encephalitis Vaccine
MMR	Measles, Mumps, Rubella
NCP	North Central Province
NIP	National Immunization Programme
PCR	Polymerase Chain Reaction
PHI	Public Health Inspector
PRNT	Plaque Reduction Neutralization Test
ULV	Ultra Low Volume
WER	Weekly Epidemiological Report
WHO	World Health Organization
WRCD	Weekly Return of Communicable Diseases

# Japanese Encephalitis A manual for Medical Officers of Health

JK ENTERPRISES Maradana - 0112 684 864



Epidemiology Unit Ministry of Health



### Foreword

Epidemiology Unit of the Ministry of Health Care and Nutrition is responsible for communicable disease surveillance and coordination of control and preventive activities. It is also responsible for managing the National immunization programme (NIP).

The success of the control of Japanese Encephalitis reflects the fruition of evidence based approaches adopted in this regard by the Epidemiology Unit. Today, it has not only been able to control the disease, but also to dynamically change strategies pertinent to disease control with special emphasis on immunization.

The ultimate benefit of this commendable work of the Epidemiology Unit with regard to JE control is reaped by the nation. Following a successfully conducted clinical trial to assess the safety and immunogenicty, live JE vaccine was introduced in the country in 2009. At a time when developing nations are struggling to sustain their vaccine budgets, shifting to a safe and immunogenic new vaccine has opened new avenues to cut down the increasing vaccine budget while ensuring the introduction and sustainability of new vaccines to the NIP.

All these timely interventions have been able to be implemented due to the intense surveillance of JE for a period of well over two decades. Sri Lanka has risen to the challenges of major outbreaks in the past and sporadic outbreaks of JE in the recent past successfully. Based on surveillance data, they have been responded rapidly with minimum consequences to the population. As such, public health practitioners in the country need to focus on the disease situation intensely even in a low endemic scenario. The role of the Medical Officers of Health and the field health staff is increasingly vital to achieve this objective. Therefore, it is my firm belief that this hand book will be of immense use to the primary health care staff to improve their knowledge on surveillance, specimen collection, lab diagnosis and immunization against JE. I extend my gratitude to the experts at the Epidemiology Unit for bearing the burden of compiling a book of this nature to update the primary health care staff. Acquired new knowledge will help further reduce the morbidity, mortality, disability and related economic implications of the JE in Sri Lanka.

Dr. Ajith Mendis Director General of Health Services

### **Preface**

It is with deep sense of pride and modesty that I recall the success Sri Lanka has achieved in JE control. JE started to affect the country in 1980s and since then, due to prompt and appropriate actions, the disease has been contained in the country.

The said success was not achieved overnight. Diligent thinking in designing appropriate disease control interventions, their efficient application, monitoring, evaluation, re drawing of strategies to suit the evolving new situations have been stated as the key factors for success in the JE control. The country has moved forward neck to neck with the industrialized nations such as Japan and Korea in JE control. Today, Sri Lanka is a success story in JE control. It is one of the few developing countries to have surveillance data for a period spanning nearly two decades.

Another feature in Sri Lanka's response was its dynamic nature of strategies. Sri Lanka implemented immunization against JE with the inactivated vaccine in 1989. Since the establishment of the AEFI system in 1990s, it has been found that AEFI of inactivated JE vaccine has affected the acceptability of the vaccine. Simultaneously, there was a problem related to the supply of the said vaccine in the global market. An additional impediment was the ever increasing cost. All these factors underlined the need of a safe, effective and cheap alternative vaccine. At this time, the WHO SAGE had recommended the live attenuated JE vaccine as an appropriate alternative. Despite available evidence on safety and efficacy, the advisory committee on communicable diseases recommended to replicate the findings in Sri Lankan children. Accordingly, a clinical trial assessing the safety and immunogenicity of the live JE vaccine among children in the Colombo district was carried out by the Epidemiology Unit with the generous sponsorship of the Program for Appropriate Technology in Health (PATH), USA. The result was evidence based instruction of the Live JE Vaccine to the NIP.

As a result of untiring work of multi-stakeholders, Sri Lanka has achieved excellent results in JE control. I wish to thank my predecessors whose vision enabled us to reach the current height. A special remembrance is required of former epidemiologists Dr. T.A.Kulatilake, Dr.M.R.N.Abeysinghe, Consultant Epidemiogist Dr. Risintha Premaratne and Dr. Nayana De Alwis, Medical Officer formerly at the Epidemiology Unit for their excellence in planning and implementation of JE control activities. I take this opportunity to thank Dr.T.S.R. Pieris, Assistant Epidemiologist for his invaluable expertise on JE immunization programme, Dr. Geethani Galagoda, consultant Virologist on her expertise on laboratory aspects of JE diagnosis. I appreciate the efforts of the Consultant Epidemiologist Dr. Geethani Galagoda for compiling the manual. Assistance rendered by the Consultant Epidemiologist Dr. Deepa Gamage in this regard also needs special mention. Last but not least PATH is appreciated for its generous sponsorship to publish this manual.

Dr. Paba Palihawadana Epidemiologist

## Japanese Encephalitis

### Introduction

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Encephalitis

Japanese encephalitis (JE) is an infection of the central nervous system caused by a virus transmitted to man through mosquitoes. Less than 1% of human JE infections are manifested as encephalitis.

JE is a major debilitating communicable disease and consequences of contracting the disease are drastic. The case fatality rate is approximately 30%. Nearly a half of the survivors of the disease suffers long term neuro- psychiatric sequelae. Therefore, invariably, there is an enormous impact of the disease on the intellectual and productive capacity and the economy of a nation.

## Virology

Japanese encephalitis virus (JEV) is a mosquito-borne *Flavivirus* closely related to West Nile and St. Louis encephalitis viruses. This virus was first isolated in Japan in 1935 from the brain of a patient dying from encephalitis. JEV is a zoonotic flavivirus belonging to the family of *Flaviviridae*. It is a single stranded, RNA virus antigenically related to several other flaviviruses including dengue. The envelope glycoprotein of the JE virus contains specific as well as cross reactive, neutralizing epitopes. The major genotypes of the virus have different geographical distributions but all belong to the same serotype and are similar in terms of virulence and host preference. Japanese Encephalitis (JE) infection is the leading cause of viral encephalitis in Asia.

Regions reported to have transmission of JE virus



Source : Adapted from Halstead SB, Tsai TF. In: Plotkin S, Orenstein W, eds. Vaccines, Philadelphia: WB Saunders Press; 2004;919-958.

## Transmission of disease

JE virus circulates in zoonotic cycles involving mosquitoes and several vertebrate species. Culicine mosquitoe species namely Culex tritaeniorhyncus, Culex gelidus are the principal vectors. However, some other culicine mosquito species such as Culex vishnui, Culex pseudovishnui and Culex fuscocephala are also responsible for the transfer of the virus to humans from amplifying hosts. Species of vector mosquitoes breed in rice fields, irrigation canals and water pools. In an urban setting, the vector can breed in contaminated water such as standing puddles, open sewers, fish ponds etc. In areas considered to be endemic for JE, up to 3% of the vector mosquitoes are infected with JEV. Although the mosquitoes prefer to feed on large domestic animals and birds, an infected mosquito may bite a human under favourable ecological conditions which facilitate the transmission of the virus to man. JEV does not spread from person to person.

Pigs and birds serve as reservoirs and amplifying hosts. They are usually unaffected by the infection. Other domesticated animals, such as horses, cattle, dogs, sheep, cows, chicken and peri-domestic rodents may become infected but do not develop levels of viraemia to support viral amplification. Man is an incidental host of the JEV. They are dead end hosts and do not contribute to the transmission cycle. In humans, following an infectious mosquito bite, initial viral replication occurs in local and regional lymph nodes. Viral invasion of the central nervous system occurs probably via blood causing infection and subsequent illness.

Immunity to JEV from previous vaccination or naturally acquired immunity reduces the risk of illness. Although most adults living in endemic areas have acquired natural immunity, adult visitors from non endemic to endemic areas are at risk of infection. Outdoor occupation and recreational exposure are also risk factors for infection. Being outdoors after sunset is a risk factor since mosquitoes commonly bite in the twilight hours. Risk for an individual traveller to endemic areas is highly variable and depends on factors such as the season, locations and duration of travel, activities of the traveller in the endemic area and the immunity to JEV (natural or acquired).

The risk of JE transmission varies by season and geographic area. Transmission of JE is generally seasonal. In the temperate climates of Asia (China, Japan, Korea, and eastern Russia) transmission occurs in autumn and summer. In these climates, JE spreads from May to September. Further south, it occurs during March to October. In the tropical areas of the Asian continent, seasonal patterns of disease may be extended or vary with the rainy season and irrigation practices. In these areas, often but not strictly, transmission of JE follows the local pattern of monsoon rains making two transmission cycles possible in a calendar year.

Transmission of JE principally occurs in rural agricultural locations where flooding irrigation is practiced. The risk of transmission is higher in rural areas, especially where pigs are raised and where rice fields, marshes and standing pools of water provide breeding grounds for mosquitoes. In many areas of Asia, these ecologic conditions may occur near, or occasionally within, urban centers also.

### **Geographical spread**

JE is the most common form of encephalitis in Asia and western pacific regions. Disease is endemic across temperate and tropical zones of Asia. In addition epidemics emerge annually in several Asian countries. It mainly occurs in countries such as Bhutan, Cambodia, China, Indonesia, Japan, Malaysia, Myanmar, Papua New Guinea, Korea, Philippines, Thailand, Viet Nam, South-eastern Russian Federation, and the Indian subcontinent. In recent decades, the disease gradually has spread to previously unaffected Asian regions and northern Australia. Except for sporadic travel-associated cases, JE is rare in Africa, Europe or America. Though it is the major cause of viral encephalitis in Asia, the disease has been successfully controlled in several Asian countries including Japan, Thailand, Korea and China through national immunization programmes.

### **Disease burden**

More than 3 billion people are now living and over 70 million children are born in JE endemic regions each year. Pediatric groups are at the greatest risk of infection in endemic areas. The annual incidence of the disease differs from country to country. Typical incidence rates of clinical JE disease in children less than 19 years in endemic areas range from < 10 to > 100 per 100000 population. Given the lack of routine standardized JE surveillance in many countries, the true incidence is under estimated.

Only less than 1% of JE cases manifest as encephalitis. Nearly 35,000 to 50,000 cases of JE are reported to WHO each year, resulting in an estimated 10,000 to 15,000 deaths annually. The case fatality rate is reported to be varied between 5-30%. In addition, 30 - 50% of survivors have significant neurological sequelae. The burden of disease, death and disability is predominantly borne by children.

Limited data indicate that JE acquired during the first or second trimesters of pregnancy causes intrauterine infection and miscarriage. Infections during the third trimester of pregnancy have not been documented to be associated with adverse outcomes in newborns. Advanced age may also be a risk factor for developing symptomatic illness after JE infection.

## **Clinical features**

Incubation period of JE infection range from 4-14 days. A majority of JE infections ends up with asymptomatic or mild symptomatic disease. On average, only 1 in 300 JE infections results in clinical illness. The clinical course of the disease is conveniently divided into three stages namely:

- 1. Prodromal stage,
- 2. Acute encephalitic stage,
- 3. Late stage,

Prodromal stage: This stage starts before the involvement of the CNS. The onset of the disease is acute and heralded initially by fever often with chills and rigors. Severe frontal or generalized head ache,myalgia, tiredness, nausea and vomiting are common. This period is variable as short as 24 hours to as long as 14 days. Later clinical cases of JE can progress to encephalitis

Acute encephalitic: This stage is characterized by altered sensorium, convulsions, stiff neck, muscular rigidity, mask like face, abnormal movement, dehydration and weight loss. Altered sensorium includes symptoms such as clouding of consciousness, excitement and confusion.

Continuous fever, nuchal rigidity, focal CNS signs, convulsions and altered sensorium are predominant. In many cases, the conditions may be worsened by coma.

Late stage: This stage is marked by recovery or persistence of signs of CNS. Increased deep tendons reflexes, thick and slow speech, aphasia and paresis are other signs and symptoms which may be present. Convalescence is usually slow.

Approximately, 30% of symptomatic JE cases result in death and onethird of the surviving cases exhibit serious neurological and psychiatric sequelae. These may include life long disability from motor problems such as limb paralysis, and behavioral changes, intellectual impairment or other neurological problems. Cognitive function is impaired by the disease ensuing poor intellectual capacity.

### Preventive and control measures:

JE virus is a part of the ecosystem with multiple hosts and vectors. Therefore, eradication of JE is not feasible. The strategy for prevention and control of JE includes major components such as awareness among general public on the prevention and control of the disease, vector control and immunization. As diagnosed patients are dead end hosts, JE is not transmissible from person to person. As such, isolation of patients and infection control measures pertaining to person to person transmission is not required when caring for patients.

### **Environmental control**

Observations from Japan, Korea and Singapore in the Asian continent have demonstrated the impact of urbanization and economic development in reducing the JE transmission. In Singapore, the urbanization of the entire country has stopped viral transmission. Reduction of vector density due to socio economic changes coupled with increased coverage of immunization against the disease are belived to have contributed to the success. Improved agricultural productivity , increasing urbanization ensuing fewer rural dwellers at risk, a decline in land area under cultivation, possible impact of agrochemicals on reduction of vector density are considered to have impacted on the reduction of disease transmission. These changes are important adjunct control measures emanating from the overall socio economic development to the effective vaccination programmes against JE. These measures are not sustainable, neither cost effective, and have limited temporary impact as a single strategy.

### Vector control:

Vector control measures cannot be expected to achieve a significant impact on overall disease burden as a single strategy. In long term, the objective of vector control measures is sustainability of low vector densities. However, vector control is an effective strategy as short term measures in outbreak situations to achieve maximum knock down of vectors.

### Short term vector control measures

Vector control measures may be useful as a short term measure, in high risk areas that are relatively small and where there is clear seasonality. A significant impact on the overall mosquito population cannot be achieved by ground application space spraying as only a limited coverage is achieved against a background of a large scale increase in vector densities and migration of mosquitoes. Larviciding is impractical due to wide spread breeding. Adulticiding by space spraying can be carried out. Though the aerial application is the only method likely to allow large scale reduction of vector densities, the use of the method is limited by the exorbitant cost. The alternative to aerial application is spraying/fogging/Ultra Low Volume (ULV) application which should cover peri-domestic animal shelters (piggeries) and vegetation in order to achieve the maximum knock down and residual insecticide activity. Applications should be carried out at dusk and dawn to coincide with the periods of maximum activity of vectors. All these applications should cover large affected areas and repetition in 10-12 days is essential to overlap the development of a new mosquito from eggs. Spraying should be evaluated by entomological investigations to ensure correct application.

For adulticiding to be effective, it must cover all mosquito habitats, which include paddy fields, puddles and drainage areas. This is practically difficult in rural paddy growing areas especially during the monsoon season. The time taken for a Culex mosquito to develop from an egg to an adult is 10-12 days. Therefore, in addition to the large area to be covered, spraying must also be repeated very frequently (every 10-12 days) to control mosquito populations. An average paddy field can produce 30,000 mosquitoes in one day presenting an incredible challenge to vector control . Indoor residual spraying has not proved to be effective as the vector is primarily an outdoor biter and fogging has only resulted in one day drop with complete recovery of adult vectors in four days.

## Long term vector control measures

Long term , non-chemical vector control options, such as water management and biological control measures, have shown a temporary drop in mosquito populations without being linked to a decrease in JE cases.

### Water management:

Water management in paddy fields and irrigation canals in agrarian settings is a long term vector control measure that may be used for sustaining low vector density. Among these measures, the most reasonable ones are as follows:

- Water management that entails periodic drying in paddy fields – Public health practitioners should convince the Paddy farmers to periodically release water accumulated in paddy fields to prevent large scale mosquito breeding. It is recommended to dry paddy fields and irrigation canals at least once a week.
- Farmers and agricultural officers should be motivated and persuaded to select paddy plants with minimum water requirements

### Use of agrochemicals:

Use of agrochemicals to control pests may have had indirect effect on vector control. However, with increasing resistance to pesticides, it is now recognized that the chemical control of vector mosquito populations of JE as a measure of disease control is not effective.

### **Biological Control:**

Use of larvivorous fish may be applicable in permanent water bodies. However, in large paddy fields periodic change of water, and the large acrages of land generate operational problems to use larvivorous fish. Other complicated operative procedures include mass scale fish rearing capability and the need of periodic release of fish to water bodies.

### Other measures:

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Other environmental measures include source reductions by drainage, filling and weeding.

Regardless of its effectiveness in controlling JE, vector control measures are important for control of many other vector borne diseases and should be maintained for control of these diseases.

### Personal protection:

The vector mosquitoes prefer to feed outdoors primarily on vertebrate hosts other than humans. They generally rest outdoors in vegetation and other shaded humid places. However, when the mosquito density increases during rainy seasons with a high density and absolute numbers of the infected mosquitoes, man mosquito contacts increase. Therefore, personal protective measures to avoid mosquito bites are important to prevent the disease during the peak hours of biting. Adopting these measures has a very high significance for adult population who are not targeted by the vaccination programme in JE endemic areas. Avoiding vegetations and shady places where mosquitoes rest during peak biting hours, minimizing outdoor activity to reduce the exposure time to mosquitoes and wearing long sleeved clothing are some practical measures that can be adopted by the people in JE endemic areas. These measures are useful as using bed nets and residual insecticide spraying are ineffective given the fact that vector mosquitoes are primarily out-door resting.

# Health Education and communication for behavioural change:

There should be simple information for general public on how to avoid exposure to mosquito bites and ways to encourage and motivate communities to engage in vector control activities. One of the Intended behavioural impacts may be use of bed nets in integrated vector borne disease control programmes with a view to avoiding man- mosquito contacts. These will not be effective in JE control since the vectors of JE prefer to feed and rest outdoors in vegetations and other shaded places.

## **Control of amplifying hosts**

Since pigs have been incriminated as the most important amplifying host of JE, control of amplifying host has been attempted in three ways; segregation, slaughtering, or vaccination of pigs. The segregation of pigs is practically impossible as a control measure. Slaughtering has a high economic impact and affects the livelihood of many families. Vaccination of pigs is costly, difficult, and time consuming. The window of opportunity for immunization is limited as pigs are often slaughtered at 6-8 months of age. Although pigs are immunized, since they are slaughtered at 6-8 months, maternal antibodies may interfere with proper immune response. Pig vaccination, therefore, has not been proved to have a significant impact on human cases of JE. In addition to the challenges of controlling pigs, many other animal hosts exist in the life cycle of JE virus. For example, breaking JE virus transmission among wadding birds will be difficult and favours enzootic cycle, makes humans vulnerable to the infection

### Immunization against JE:

Immunization against JE is the single most cost effective strategy for control and prevention of JE. Many countries have demonstrated that incidence rates of JE in endemic areas with high immunization rates have been dramatically reduced and sustained at lower rates. Currently, there are 3 important types of JE vaccines in large scale use :

- The mouse brain derived , purified, inactivated vaccine based on either the Nakayama or Beijing strains of the JE virus
- 2. The cell culture derived inactivated JE vaccine based on the viral Beijing P3 strain
- 3. The cell culture derived live attenuated JE vaccine based on the SA 14-14-2 strain of the JE virus.

## Japanese Encephalitis in Sri Lanka

The JE virus was first isolated in 1968 in Sri Lanka at the Medical Research Institute even though there were speculations about a possible outbreak of JE in 1948. The first major outbreak was experienced in 1984 (November) - 1985 (February) in the North Central Province (NCP) in Anuradhapura district. In this outbreak, a total number of 385 individuals were reported to have contracted JE and 64 of them died with a case fatality rate (CFR) of 17%. Predominantly affected age groups in this outbreak were 5-9 years and 20-29 years. The sex ratio (male: female) affected was found to be 2:1. In the following year too, the outbreak occurred in the districts of Anuradapura and Polonnaruwa in the NCP with the extension of the outbreak to the adjoining districts of Kurunegala and Puttalam in the North Western Province. Incidentally, this was the largest outbreak reported so far with 812 cases, 192 deaths with a CFR of 24%. Since then, JE cases have been identified from various parts of the country.

Outbreaks of JE were consistent with the rainy season in particular with the North-East monsoonal rains (November to February). During this period, vector density tends to increase due to water logging in paddy fields, irrigation canals and shallow ditches. Deforestation for agricultural settlements, rapid expansion of stretches of paddy fields, extension of the irrigation network by reconstruction of new canals and restoration of ancient remnants of canals in affected areas were identified as attributable factors for the emergence of JE vector mosquitoes in abundance. The attraction of a large contingent of non immune, susceptible migrants to the dry zone under the government colonization programme aimed at expanding agriculture in the dry zone enabled the emergence of JE in outbreak proportion. Furthermore, piggeries in closer proximity to residential areas provided amplifying hosts to enable the spread of JE in human dwellings.

Until 1988, the major strategy for control of JE in endemic areas in Sri Lanka was vector control. Based on empirical evidence of successful JE control in Japan and Korea through immunization which appeared to be the most cost effective, public health tool to cope with this emerging challenge of JE, the Epidemiology Unit of the Ministry of Health initiated an immunization programme against JE on phase basis in 1988 in Sri Lanka. Children in the age group of 1-10 years were targeted for immunization against JE. They were vaccinated with four doses of the Nakayama strain of the inactivated JE vaccine during the inter-epidemic period. In 1988, 409888 doses had been administered to the eligible children.

The results of the immunization campaign were far reaching. Over the years, incidence of JE decreased with increasing immunization coverage. However, the disease was spreading to new areas with previously low levels of enzootic transmission. Occasional outbreaks were reported in these districts. The last such outbreak was reported in the Ratnapura district in 2002. These findings highlighted the need for expanding the immunization programme to other potentially vulnerable areas. Ultimately, the programme was existent in the 17 districts in the country. These 17 districts included all districts in the Western, Southern, North Central, North western, Eastern, Jaffna and Vavuniya in the Northern province, Ratnapura in the Sabaragamuwa province and Matale in the central province.

Though Sri Lanka has continued the JE immunization programme with the Nakayama strain, it was replaced with Beijing strain in 1992

and continued till 2006. The success of the immunization against JE in Sri Lanka is reflected in the fact that since 1988, incidence of JE has decreased drastically with the increased coverage of immunization. Since 2003, only sporadic JE cases have been reported from different parts of the country. Since of late, one notable epidemiological observation has been the changing age spectrum of the confirmed JE cases towards old ages.

### Immunization of pigs against JE in Sri Lanka.

A programme for immunization of pigs was carried out in some areas by the Department of Animal Production and Health (DAPH), with the assistance of Public Health Veterinary Services of the Ministry of Health in the past. However, currently this programme is not conducted considering its limited effectiveness.

## Surveillance of Japanese Encephalitis

## WHO recommended surveillance standards for JE

Surveillance is defined as the systematic and ongoing collection, orderly consolidation and evaluation of pertinent data with prompt dissemination of the results to those who need to know and in particular to those who are in a position to take action.

Surveillance data is important for decision making. It guides policy and strategies in JE control in a country. A country is able to identify high risk geographical areas and populations to design and implement control activities based on surveillance data. It points out areas where immunization coverage should be improved while enabling assessment of the effectiveness of the JE vaccine and impact of vaccination on the disease burden. Surveillance is imperative to monitor the surveillance  $\Im C$  and the performance of the laboratory. Thus it is obvious that 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.

According to the WHO surveillance standards for JE, comprehensive syndromic surveillance for acute encephalitis syndrome with aggregate reporting is recommended in all Asian countries. In sentinel hospitals, surveillance should be case-based with specimens collected for laboratory confirmation. In Asian countries where a high level of JE control has been achieved, surveillance should be casebased throughout the country and include laboratory confirmation of all suspect cases. The surveillance of JE should be carried out through out the year.

Infection caused by the JEV may be asymptomatic, or manifest as a febrile illness, meningitis, myelitis or encephalitis. Encephalitis is the most commonly recognized presentation. More often than not, it is clinically indistinguishable from other causes of an acute encephalitis syndrome (AES). Clinical syndromic surveillance, therefore, is used to identify patients with AES. Subsequently, among these patients JE is confirmed using standardized laboratory techniques.



One obstacle encountered in surveillance is that due to lack of availability of JE diagnostics particularly in rural areas, laboratory confirmation of JE is not always possible. Such a limitation should not underestimate the syndromic AES surveillance in a country. As frequently AES data are parallel to JE infection trends, some countries perform AES surveillance nationally and use diagnostics in selected sentinel sites to provide additional information on JE.

Two approaches have been used to collect data in JE surveillance namely;

## (I) Syndromic surveillance of AES

Specific JE surveillance including Laboratory confirmed and epidemiologically associated JE cases.

The WHO has recommended surveillance case definitions of AES and case classifications to be used in syndromic surveillance.

## **Clinical case definition of AES:**

Clinically, a case of acute encephalitis syndrome (AES) 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 seizures ). Other early clinical findings may include an increase in irritability, somnolence or abnormal behaviour greater than that seen with usual febrile illness.

A case that meets the clinical case definition for AES is a suspected JE case. Suspected cases should be classified in one of the four following ways.

### 1. Laboratory-confirmed JE

A laboratory confirmed JE cases is defined as a suspected case that has been laboratory-confirmed as JE. Laboratory confirmation of a JE virus infection includes:

 Presence of JE virus-specific IgM antibody in a single sample of cerebrospinal fluid (CSF) or serum as detected by an IgM-capture ELISA specifically for JE virus

### or any of the following:

• Detection of JE virus antigens in tissue by immunohistochemistry;

### OR

• Detection of JE virus genome in serum, plasma, blood, CSF or tissue by reverse transcriptase polymerase chain reaction (PCR) or an equally sensitive and specific nucleic acid amplification test;

#### OR

• Isolation of JE virus in serum, plasma, blood, CSF or tissue;

### OR

• 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.

To eliminate the possibility of cross reactivity with other flaviviruses circulating in the geographical area, further confirmatory tests are required when there is an ongoing dengue or other flavivirus outbreak, when vaccination coverage is very high or in cases in areas where there are no epidemiological and entomological data supportive of JE transmission.

### 2. Epidemiologically associated / probable JE case:

During an epidemic of JE, laboratory confirmation of 5- 10 cases would be adequate and further laboratory confirmation may not be necessary. A suspected case that occurs in close geographic and temporal relationship to a laboratory-confirmed case of JE, in the context of an outbreak is considered epidemiologically- associated / probable JE cases.

### 3. AES - other than JE;

A suspected case in which diagnostic testing is performed and an aetiological agent other than JE virus is identified.

### 4. AES - unknown cause:

A suspected case in which no diagnostic testing is performed or in which testing was performed but no aetiological agent was identified or in which the test results were indeterminate.

## (II) Sentinel surveillance:

JE is a severe clinical illness that is commonly cared for in a hospital setting. Therefore, hospital-based sentinel surveillance at selected sites is a useful way to begin assessment of the JE disease burden. It enables identification of suspected JE cases (AES cases) and laboratory confirmation for case classification (confirmed JE, AES –other than JE, AES-unknown cause, probable JE) .In sentinel hospitals, case based surveillance is recommended with specimens being collected for laboratory confirmation. Since hospital-based sentinel surveillance uses only specific sentinel sites, this method is less costly and

complex than more widespread testing. Individual countries are able to increase the number of sentinel sites depending upon the available resources for surveillance.

## Performance indicators of surveillance quality:

The WHO has recommended following targets for countries with a well established AES surveillance system.

### 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%

Those countries which have commenced JE surveillance may set intermediate targets for surveillance.

WHO has developed indicators, to be used as managerial tools to identify areas where corrective action is needed, (Table 2) for countries where a high level of JE control has been achieved.

## Table 2 :

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Indicators to identify areas where corrective action is needed

Indicator	Target
Percentage of all suspect cases for which specimens were collected ( in a nationwide case based surveillance )	> 80%
Percentage of CSF/serum samples reaching laboratory in adequate con- dition ( transported using reverse cold chain )	>80%
For all tests, laboratory results re- ported < 1 month after receipt of specimen	> 80%

## Acute Encephalitis Syndromic surveillance in Sri Lanka

Routine surveillance on encephalitis (Notification)

Notification of communicable diseases (CD) in Sri Lanka dates back to the colonial period. The Quarantine and Prevention of Diseases Ordinance acts as the legislative foundation for routine notification of CD. The ordinance includes the list of notifiable diseases including encephalitis. According to this ordinance, all medical practitioners and persons professing to treat diseases and attending to patients suspected of encephalitis should notify the case on a notification of a communicable disease form (H 544) to the relevant MOH. Notification of a patient with a notifiable disease initiates a regulated flow of activities in the field. All H544 forms received at MOH offices are entered in the Notification Register of the MOH office and handed over to the relevant area Public Health Inspector (PHI) in whose area the notified encephalitis patients reside and may have contracted the disease. Receipt of these notification forms are then noted in the Letter Inward Register of the relevant area PHI and investigated personally by the officer as soon as possible and ideally within 7 days of receipt of the notification form. The house of the patient is visited by

the PHI and relevant additional information is obtained from the patient, his/her medical records, his/her family and the environment. The probable diagnosis of the notified encephalitis cases can be either confirmed or discarded following these investigations. For confirmed cases the PHI is responsible to carry out control and preventive measures related to the disease following the investigation.

Another form, Communicable Diseases Report (CDR) Part I – H411 (Annexure 1) is completed for each case investigated and this is also noted in the Letter Outward Register of the PHI. Data from all confirmed cases are then entered in the Infectious Disease Register at the PHI office. Completed CDR part I- H 411 and H 544 (Annexure 2) forms are returned to the MOH office following this series of activities carried out by the PHI. At the MOH office, details from the above forms on each encephalitis case notified are used to update the Office Notification Register and if confirmed, entered in the Office Infectious Disease Register (H700). Based on the Form "CDR part I- H 411 " sent by the PHI. Communicable Disease Report Part II- H411a (Annexure 3) is completed for each confirmed encephalitis case at the MOH office. Details of investigation status of encephalitis cases are consolidated in the Weekly Return of Communicable Diseases (WRCD - H 399) (Annexure 4). The WRCD with the completed CDR Part II - H 411a are posted to the Epidemiology Unit on every Saturday of the week.

All notified cases of encephalitis during the week of concern is entered in in the Weekly Return of communicable Diseases (WRCD)- H 399. Additionally, in the weekly summary (part II) of the WRCD, cages relevant to "encephalitis cases notified earlier and awaiting investigation at the beginning of the week", "cases decided as unrtraceable during the week", "cases decided as belonging to other MOH areas during the week", "cases confirmed as non encephalitis during the week", "cases confirmed as encephalitis during the week" and "encephalitis cases awaiting investigation at the end of the week" are completed. The completed WRCD is sent to the Epidemiology Unit. Data on encephalitis received through WRCD from MOH areas in the country are entered in a central database at the Epidemiology Unit and consolidated at the end of every week. These consolidated data in the form of a summary report is published in the Weekly Epidemiological Report (WER), which is circulated to all health institutions in the country completing the feedback link in the national disease notification chain. Data on notified encephalitis cases are also summarized quarterly in the Quarterly Epidemiological Bulletin published by the Epidemiology Unit. Both WER and the Quarterly Epidemiological Bulletin are available at the official website <u>www.epid.gov.lk</u>. Also, the Annual Health Bulletin publishes cumulative data on Japanese encephalitis obtained from WRCD every year.

## Special investigations on encephalitis

Further to the field investigations during routine surveillance of encephalitis, special investigations are carried out. Special investigations are aimed at obtaining more detailed data than that is available through the routine preliminary field investigations for this disease. Information targeted through special investigations includes patients' demographic information, information on the disease, its clinical presentation, laboratory investigations, clinical conclusions, vaccination status and risk factors for JE. It helps to select the confirmed cases out of initially notified clinically suspected cases and identify potential contributory factors associated with the disease status

According to the general circular No: 01/42/2008, special investigations on encephalitis should necessarily be carried out by the Medical Officer of Health (MOH)/ Additional Medical Officer of Health (AMOH) or any other Medical Officer. The outcome of the investigation should be reported in duly completed case investigation form for surveillance of encephalitis (EPID/DS/JE/2010) (Annexure 5). Under no circumstances, this form should carry the signature of a Public health inspector or any officer other than the MOH / AMOH or any other Medical Officer.

For the ease of surveillance of encephalitis at the field level, the Epidemiology Unit has simplified the standard surveillance case definitions of AES.

### A suspected Japanese Encephalitis case

A case that is compatible with the surveillance case definition of acute encephalitis.

Case Definition:

An illness with an acute onset of possible encephalitis including high fever and altered mental status .

### A probable Japanese encephalitis case

A suspected case with presumptive laboratory results.

An encephalitis case in which CSF contains 5- 1000 cells/mm3 (pleocytosis).

### A confirmed encephalitis case due to JE virus

A suspected case with confirmatory laboratory results is considered as a confirmed encephalitis case due to JE virus.

## Laboratory criteria for diagnosis of Japanese Encephalitis Presumptive:

- Fourfold or greater rise in JE virus-specific IgG antibody in paired sera (acute and convalescent phases), ELISA, haemagglutination inhibition test or virus neutralization test, in patient with no history of recent yellow fever vaccination and where cross-reactions to other flaviviruses have been excluded.
- JE virus specific IgM antibody in single blood sample in late acute phase or early convalescence.

### Confirmatory :

• JE virus specific IgM antibody in the CSF by IgM capture ELISA

### or

• Detection of the JE virus, antigen or genome in brain, spinal cord by immunochemistry or immunoflourescence or PCR.

AES surveillance information are often used as a proxy for estimating the burden of JE since, frequently, AES data are parallel to JE infection trends. Information on laboratory confirmed JE obtained through laboratory surveillance data disseminated by the Medical Research Institute compliments AES surveillance information.

## Uses of JE surveillance data in Sri Lanka

In Sri Lanka, Surveillance data are used to determine the disease burden and epidemiology of JE in endemic and non endemic areas. Based on surveillance data, JE immunization programme was designed in Sri Lanka as the single most cost effective intervention against JE. It assisted defining the most vulnerable target groups for JE immunization. Detection and investigation of every single case of vaccine preventable diseases is vital as those cases will indicate the need for further strengthening the national immunization programme. In this regard, AES surveillance data have been proved to be extremely useful in monitoring and evaluating the JE immunization programme and changing its policy directions.

AES surveillance information, JE in particular, helps forecasting JE outbreaks and expansion of JE immunization to new districts based on the transmission of the disease. Continued JE surveillance is also useful to determine the effectiveness of the live attenuated JE vaccine which was recently introduced in Sri Lanka. Further, continued disease surveillance will guide the necessity of introducing an additional dose of live attenuated JE vaccine in the future.

# Japanese encephalitis surveillance information in Sri Lanka

Epidemiology Unit carries out syndromic surveillance of Acute Encephalitis cases. Surveillance data related to encephalitis obtained weekly through the WRCD from 2002-2010 are given below.

Table 3 :	Distribution of reported encephalitis cases
	in 2002-2010 by districts

Districts	Year								
	2002	2003	2004	2005	2006	2007	2008	2009	2010
Colombo	05	02	03	02	06	11	15	13	17
Gampaha	07	11	11	03	10	30	20	23	30
Kalutara	04	00	04	03	08	06	14	16	15
Kandy	00	07	02	04	09	06	12	08	06
Matale	00	01	00	03	07	06	06	04	08
Nuwareliya	00	03	00	00	00	02	06	02	01
Galle	05	08	05	04	03	13	23	10	10
Hambantota	08	05	00	01	09	06	08	08	07
Matara	02	05	01	01	10	10	14	09	08
Jaffna	02	02	03	02	04	02	04	03	10
Kilinochchi	00	00	00	00	00	00	00	00	00
Mannar	00	00	01	00	00	00	06	01	02
Vavuniya	00	00	02	03	05	04	03	25	03
Mullaithivu	00	01	00	00	01	08	00	00	00
Batticaloa	02	00	02	02	03	12	08	15	05
Ampara	00	02	00	00	00	00	01	01	01
Kalmunai	01	04	03	00	01	04	02	02	03
Trincomalee	04	04	02	00	01	04	03	04	14
Kurunegala	03	07	07	03	06	09	18	13	21
Puttalam	00	05	06	03	03	17	12	07	09
Anuradhapura	01	04	03	02	09	10	10	10	11
Polonnaruwa	04	03	00	00	02	03	01	04	02
Badulla	00	03	09	00	04	07	08	05	01
Monaragala	00	00	06	01	07	02	04	02	02
Ratnapura	17	82	36	21	19	20	35	24	08
Kegalle	02	05	04	02	03	11	28	10	19
Total	181	164	108	60	130	203	259	219	213

Source: WRCD (Epidemiology Unit)

Based on case-based investigation (special surveillance) of routinely reported AES cases by MOH, all cases that meet the surveillance case definition of AES are considered as suspected JE cases. Of these cases, number and proportion of suspected JE cases with CSF findings compatible with viral encephalitis are given in the table 4.

Table 4 : Distribution of suspected JE cases with CSF findings	
compatible with viral encephalitis	

Year	No. (%) of Probable viral encephalitis
2006	39 (42.3)
2007	49 (24.2)
2008	46 (40.7)
2009	35 (48.6)
2010	39 (41.9)

It has to be mentioned that the cases compatible with viral encephalitis should be more than what is given in the table. This is due to the low special investigation rates and inadequate laboratory (CSF) findings in special investigation forms completed and submitted to the Epidemiology Unit by the MOH.

Based on results of aetiological diagnostic testing, suspected JE cases are classified as laboratory confirmed JE cases. Laboratory confirmation of Japanese Encephalitis is carried out at the Medical Research Institute. However, a majority of AES cases are not subject to laboratory confirmation for JE. Hence, they are classified as suspected JE cases with an unknown cause.

Laboratory confirmed JE cases , deaths and the JE specific morbidity rate and case fatality ratio calculated based on confirmed JE cases from 1985 to 2010 are given in the figure 1 and table 5.

## Figure 1 : JE specific morbidity Rate [per 100,000] & Case Fatality Ratio (%), 1985-2010



TABLE 5 : Cases, Deaths and Case Fatality Rate (CFR) of Japanese Encephalitis 1990 – 2010

Year	Japanese Encephalitis						
	Ca	ases	Deaths	CFR (%)			
	No.	No. Rate *					
1990	387	2.3	43	11.1			
1991	325	1.9	25	7.7			
1992	291	1.7	27	9.3			
1993	289	1.6	52	18			
1994	230	1.3	41	17.6			
1995	173	1	32	18.5			
1996	307	1.7	44	14.4			
1997	164	0.9	19	119			
1998	122	0.7	3	2.5			
1999	102	0.5	3	2.9			
2000	83	0.5	2	2.4			
2001	66	0.4	9	13.6			
2002	113	0.6	15	13.2			
2003	133	0.7	20	15			
2004	129	0.7	9	6.9			
2005	65	0.3	6	9.2			
2006	26	0.1	1	3.8			
2007	39	0.2	0	0			
2008	31	0.2	6	19.4			
2009	34	0.2	4	11.8			
2010	27	0.1	3	11.3			

There has been a clear reduction in JE specific morbidity rate since the initiation of JE immunization programme in 1988. However, there were occasional outbreaks reported in districts, where immunization was not carried out, from time to time.

Special surveillance of AES has demonstrated seasonality of both AES and confirmed JE cases in Sri Lanka. Temporal distribution of AES and JE cases in Sri Lanka by months during 2006-2010 is given in the figure 2 and 3.

FIGURE 2 : Distribution of Reported AES cases by months during 2006-2010



FIGURE 2 : Distribution of Confirmed JEcases by months during 2006-2010



Despite the fact that AES cases are detected through out the year, two peaks of increased AES reporting are prominent. The biggest peak appears to have occurred from November.

A similar picture is visible for confirmed JE cases too. Although JE cases are detected through out the year, number of JE cases tends to increase during the period from November to February. This period is consistent with the North Eastern monsoon in Sri Lanka with a moderate to high rain fall.

Although JE was reported in the North Central Province in 1985-86, gradually it started to spread to other areas in later years. However, the spatial distribution of JE has dramatically changed since the introduction of and achieving coverage for JE vaccination. Given below is the spatial distribution of JE cases in Sri Lanka from 2006-2010.

## Table 6 : Distribution of laboratory confirmed JE cases by districts from 2002 -2010

	Year								
Districts	2002	2003	2004	2005	2006	2007	2008	2009	2010
Colombo	22	20	28	13	12	10	00	03	0
Gampaha	05	00	03	02	01	04	02	08	0
Kalutara	00	00	00	00	00	01	04	04	0
Kandy	01	05	02	00	03	02	00	01	00
Matale	00	00	00	02	00	00	00	00	0
Nuwareliya	00	00	00	00	00	00	00	01	C
Galle	01	02	02	01	00	01	02	01	04
Hambantota	00	00	00	01	00	01	01	00	) (
Matara	00	00	00	00	00	01	00	00	0
Jaffna	00	01	02	00	01	01	00	00	00
Kilinochchi	00	00	00	00	00	00	00	00	0
Mannar	00	00	00	00	00	00	00	00	0
Vavuniya	00	01	00	00	00	00	01	00	0
Mullaithivu	00	00	00	00	00	01	00	00	0
Batticaloa	08	04	08	00	00	01	00	01	0
Ampara	00	00	00	00	00	00	00	00	0
Kalmunai	00	00	00	00	00	00	00	02	0
Trincomalee	01	04	01	00	00	00	01	02	0
Kurunegala	00	00	03	03	01	00	01	00	0
Puttalam	00	00	00	02	00	00	01	01	0
Anuradhapura	01	03	06	00	05	09	00	00	) (
Polonnaruwa	00	01	00	00	00	01	01	00	) (
Badulla	00	01	00	00	00	00	00	00	0
Monaragala	00	00	00	00	00	00	00	00	0
Ratnapura	05	10	04	08	03	05	04	02	0
Kegalle	00	00	00	01	00	01	01	04	0
Location not detected	00	00	00	00	00	00	12	04	02
Total	44	52	59	33	26	39	31	34	27

Source: Special surveillance of encephalitis (EPID/DS/JE/2007)

In 1980s when JE occurred in outbreak proportions, pre dominantly affected age groups were children below 10 years of age. Based on the susceptibility of this age group to the disease, the JE immunization programme targeted children in the age group of 1-10 years for

immunization. Consequent to the expansion of the immunization programme to 18 districts with a high immunization coverage, there has been a shift in the vulnerable population to JE. Age distribution of reported JE cases from 2006-2008 is given in the table 7.

Table 7 : Distribution of laboratory	confirmed JE cases in Sri Lanka
by age from 2006-2010	

	Year									
Age group	2006	2007	2008	2009	2010					
<1 year	01(03.8%)	1 (2.6%)	0 (0.0%)	2(5.9%)	1(3.7%)					
1-4	03(11.4%)	3 (7.8%)	1 (3.2%)	4(11.8%)	6(22.2%)					
5-9	00 (0%)	2 (5.2%0	1(3.2%)	2(5.9%)	1(3.7%)					
10-14	3 (11.4%)	3 (7.8%)	1(3.2%)	2(5.9%)	1(3.7%)					
15-19	1(3.8%)	1 (2.6%)	2 (6.4%)	2(5.9%)	2(7.4%)					
20-24	1(3.8%)	3 (7.8%)	5(16.0%)	6(17.5%)	1(3.7%)					
25-29	1(3.8%)	0 (0%)	1 (3.2%)	3(8.8%)	1(3.7%)					
30-34	1(3.8%)	6 (15.6%)	1(3.2%)	3(8.8%)	3(11.1%)					
35-39	1 (3.8%)	2 (5.2%)	1(3.2%)	0(0.0%)	1(3.7%)					
40-44	0(0%)	1(2.6%)	3 (9.6%)	1(2.9%)	0(0.0%)					
45-49	3(11.4%)	2 (5.2%)	3 (9.6%)	3(8.8%)	0(0.0%)					
50-54	3 (11.4%)	5 (13.0%)	0 (0.0%)	1(2.9%)	3(11.1%)					
55-59	1(3.8%)	1(2.6%)	2 (6.4%)	1(2.9%)	2(7.4%)					
>60	4(15.2%)	5 (13%)	7(22.4%)	2(5.9%)	5(18.5%)					
Unknown	3(11.4%)	4 (10.4%)	2 (6.4%)	2(5.9%)	0(0.0%)					
Total	26	39	31	34	27					

Confirmed JE cases have been predominantly detected among those who were above 30 years of age. They were unlikely to have been exposed to the JE immunization initiated in 1989. It also reflects the shifting of age distribution towards adults in the post JE vaccination era,

In the post vaccination period, cases are being reported predominantly among those who were not exposed to immunization. Immunization status of the reported JE cases in 2008 - 2010 are given in the table 8. Table 8 : Distribution of laboratory confirmed JE cases by JE Immunization status from 2008-2010

			2008		
Sex	Age group	Immunized	Non immunized	Unknown	Total
Male	< 10Y	1	1	0	2
	11-20Y	0	1	1	2
	21-30Y	0	1	1	2
	31-40Y	0	0	0	0
	>40Y	0	1	1	2
Male Total		01(12.5%)	04 (50%)	03(37.5%)	08 (47 1%)
Eomalo	<10V	0	1	0	1
Temale	11 201	0	0	0	0
	04 20V	0	4	0	1
	21-301	0	0	4	1
	31-401	0	0	1	1
	>40	0	4	2	6
emale l'otal		U	06(66.6%)	03 (33.3%)	09 (53.9%)
Grand Total		01(5.8%)	10(58.8%)	06 (35.3%)	17
			2009		
Sex	Age group	Immunized	Non immunized	Unknown	Total
9CX	Agegroup	mmullizeu	Non minumizeu	UNKIOWI	Total
Malo	< 10V	0	2	3	6
maie	< 10T	0	3	3	6
	11-201	0	3	2	5
1	21-304	0	0	3	3
	31-40Y	0	2	0	2
	41-50	0	0	0	0
G	>50Y		4	2	2
	unknown	10	2	110004610.1014020	
Male Total		0	8(44.5%)	10(55.5%)	18 (100%)
Female	<10Y	0	1	1	2
	11-20Y	0	0	0	1
	21-30Y	0	5	1	6
	31-40Y	0	0	1	1
	>50Y	0	6	0	6
Female Total		0	12(75%)	4(25%)	16 (100%)
Total		0	20(58.8%)	11(32.4%)	34 (100%)
			0040		
Sex	Age group	Immunized	Non immunized	Unknown	Total
	1.90 9.000				
Male	< 10Y	0	2	5	7
	11-20Y	0	0	3	3
	21-30Y	0	0	2	2
	31-40Y	0	0	1	1
	41-50	0	0	1	1
	>50Y	0	2	1	3
	unknown	0		1.51	00(00%)
Male Total			04(23,5%)	13(76.4%)	17(100%)
Female	<10Y	0	0	1	1
1 onnaro	11.20Y	0	0	0	0
	21.30V	0	0	0	0
	21-301	0	0	2	2
	51-4UT	0	0	3	3
	>00Y	U	0	6	6
	UnKnown	U	0	0	
emale Total		0	0	10	10(100%)
Total		0	04(14.8%)	23(85.1%)	27 (100%)

# Investigation of suspected Acute Encephalitis outbreaks in Sri Lanka

Outbreak is defined as an occurrence of a disease in excess of the expected frequency in a given area, among a specific group of people over a particular period of time or two or more epidemiologically linked cases( of the same illness) in a short period. A MOH comes to know about an outbreak of encephalitis either through the indicator based or event based surveillance systems. In the Sri Lankan context, timely analyzed routine acute encephalitis notifications from hospitals help a MOH to identify clusters of acute encephalitis in his area of jurisdiction. The other way of obtaining less valid yet rapid information on clusters of acute encephalitis is through rumours and ad hoc reports via informal information channels such as print / electronic media, health workers and the general public. Once information have been received about clusters of encephalitis, the next task of a MOH is to determine if this is an outbreak (Establishing the existence of an outbreak). For this purpose, the observed frequency of AES cases has to be compared with the expected number of AES cases for the given locality, population and time. Each MOH is supposed to establish the epidemic threshold of AES cases based on previous surveillance information in his area. Once the epidemic nature of the disease has been confirmed, it is necessary to establish what disease is exactly occurring in the MOH area (verifying the diagnosis). Reviewing and summarizing clinical and laboratory findings of the cases that have already been reported, consulting clinicians and meeting patients facilitate verification of the diagnosis. Further, it enables describe the clinical spectrum of the encephalitis cases reported and development of a case definition. While reviewing available laboratory findings, a MOH may have to organize collecting specimens from other patients and sending them to the National JE reference laboratory at the MRI to verify the diagnosis. The required specimens, technique of collection, quantity of materials for testing etc are mentioned elsewhere in this manual. By this time, the MOH has established the existence of an

outbreak, verified the diagnosis and described the clinical spectrum of the disease. The subsequent step is developing a case definition (possible, probable or confirmed) to determine the likelihood of the victim being an encephalitis patient. In the early stage of the investigation, the focus will be on a loose case definition. When the focus is sharply on a hypothesis or the hypothesis requires testing, a rigorous case definition is used. Subsequently, using this case definition, the MOH will look for additional cases through active or stimulated passive surveillance or active case finding. It enables identify patients affected by the disease, their characteristics and quantification of the outbreak (case finding and case counting). In this process, identification, demographic, clinical, risk factor and JE immunization data are collected from patients. These collected data are entered into a data base by the MOH and this is referred to as a line listing. Using this line listing, the next step is to describe the outbreak by time, place and person to develop a working hypothesis regarding the causative agent, mode of transmission of the outbreak, exposures/risk factors and the susceptible population (Performing descriptive epidemiology). Description of patients by place is done by preparing a spot map manually, using a software for mapping or Geographic Information System (GIS). The time relationship of the outbreak is depicted by an epidemic curve (Histogram of number of cases by date or time of onset). It enables identifying the index case, incubation period, determining the type of the outbreak, stage of the outbreak, the likely period of exposure (identify the source of infection) and declaring the outbreak closed. Description by persons will help identify the "at-risk population". By this time, the MOH has a working hypothesis of the outbreak so as enable him to initiate tentative measures for the outbreak management.

nvestigation of AES outbreaks

If the MOH is competent enough or else with the support of the Regional Epidemiologist or consultant epidemiologists at the national level, he may test the formulated hypothesis using analytical epidemiological techniques (performing analytical epidemiology). Observational studies ( case control or cohort ) may be conducted for this purpose and the type of study will be dependent upon factors such as feasibility, cost etc. This process will epidemiologically point out the most likely cause/s of the outbreak. Conducting environmental studies including entomological surveys will provide additional supplementary data to substantiate and explain the epidemiologically confirmed hypothesis. Based on the investigation, now it is possible to implement evidence based control measures and evaluate the effectiveness of the response. Depending upon the source and mode of transmission of the AES outbreak ( JE, West Nile, Nipah virus etc) appropriate long term and short term control and preventive measures have to be implemented. The relevant strategies for control and prevention of JE outbreaks have been described in details in the section "preventive and control measures" in the chapter 1.

## Laboratory Diagnosis of JE infection

The laboratory diagnosis of Japanese encephalitis (JE) infection is necessary as the clinical features of the infection indistinguishable from other causes of an Acute Encephalitic Syndrome.

Sero-confirmation is conducted in sporadic cases and at the initial phase of an outbreak. However laboratory diagnosis is not feasible once an outbreak has been established. Those serology is not useful for the clinical management of the patient, it is useful for a retro-spective diagnosis and epidemiological purposes.

The laboratory tests for Japanese Encephalitis are of 2 types.

- 1. JE specific aetiological diagnosis tests
  - Demonstration of IgM antibody in CSF Demonstration of IgM antibody in serum Demonstration of rising IgG antibody titer in serum Virus isolation Molecular testing
- Non specific diagnostic tests such as CSF analysis

## Non specific diagnostic tests

### **CSF** analysis

The CSF is clear with elevated tension. There are increased lymphocytes and elevated protein levels with a normal glucose level.

### **Collection of samples**

### CSF

The sample should be collected after the 5<sup>th</sup> day of the illness. 0.5 - 1.0 ml of CSF is collected in to a labeled, sterile, screw capped container. It is collected as the 4<sup>th</sup> sample during a lumbar puncture. The CSF has to be transported immediately to the Department of Virology, Medical Research Institute. The sample does not have to be refrigerated, unless there is a delay in transport. If there is any delay, it

should be stored at  $4^{0}\text{C}\,$  and transported with ice packs in a reverse cold chain.

### Serum

Detection of IgM - A single sample of serum should be collected after the 5<sup>th</sup> day of illness.

Detection of IgG - Paired blood samples collected 7-14 days apart are required to demonstrate a four-fold antibody rise / seroconversion. The acute serum sample should be obtained as soon as possible during the course of illness, and no later than 5-7 days after onset.

About 2-5 ml of venous blood should be collected into a labelled, clean (preferably sterile), dry, screw capped container. The sample should be kept at room temperature for 30 min to 1 hour for a blood clot to form and retract. The serum should be separated and sent to the hospital laboratory to be transported to the national reference laboratory. If a delay in transport for >48 hours is anticipated, serum should be stored at  $+4^{\circ}C$  and transported with ice packs in a cold chain.

## Important:

All specimens should be accompanied with a duly filled request form. (Date of onset of illness, Date of onset of illness, H/O JE vaccination and dates of vaccination should be included.)

## variables for sample request form

Date of onset of illness	
Date of onset of illness	
History of JE vaccination	
Date of JE vaccination	

## Tests for aetiological diagnosis

## Demonstration of IgM antibody in CSF

The diagnostic test is the demonstration of JE specific IgM antibody in the CSF. The sensitivity of the IgM test in CSF is about 80-90%. Antibody demonstration is done by the IgM capture enzyme linked immunosorbent assay (EIA) method. Specific antibody is demonstrated in CSF in approximately 75% of the patients by the 3<sup>rd</sup> day of infection and 100% of patients by the 7<sup>th</sup> day of infection. There will be detectable antibody for about 3 months after the infection. There is no cross-reactivity with other infections.

## Demonstration of IgM antibody in serum

Specific IgM antibody can be demonstrated in the serum by the same method as CSF. The sensitivity of the test is about 10%. Like in CSF, 75% of the patients will be positive by the  $3^{rd}$  day and all patients by the 7<sup>th</sup> day of infection. The IgM antibody will persist in blood for about 3 months after infection.

## Demonstration of IgG antibody in serum

A rising IgG antibody or seroconversion of JE antibody in paired blood samples can be demonstrated by Haemagglutination Inhibition test (HAI). A four-fold rise in antibody titer or presence of antibody in the second or convalescent sample indicates an acute infection. False positive reactions can be seen with other flaviviral infections like dengue and West Nile virus.

Plaque Reduction Neutralization test (PRNT) test Plaque Reduction Neutralization test (PRNT) is another test that can be used. It is the gold standard for neutralizing antibody in JE.

## Virus isolation

This test is available only as a research tool.

### Molecular testing

Detection of the JE viral genome by PCR is a very sensitive and reliable test. The CSF is the best sample and has to be collected within the first 4 days of illness. Vaccines against Japanese encephalitis Mouse brain derived, purified and inactivated JE vaccine:

## Introduction:

Inactivated JE vaccine is made from either the Nakayama strain or the Beijing strain of the JE virus after being propagated in mousebrain tissue, purified and formalin inactivated. This vaccine has been used successfully in Taiwan, Japan, the Republic of Korea, Thailand and Viet Nam. Nakayama strain protects against JE virus strains from different Asian regions. However, since the Beijing-1 strain induces stronger, broader neutralizing antibodies and because of the high antigen yield of the Beijing strain, Nakayama strain has been replaced with Beijing strain. Wider use of Beijing strain does not pose problems as there is no significant difference between these two strains in inducing protective immunity and being efficacious in humans. Sri Lanka has been using both Nakayama (from 1988-1992) and Beijing (from 1992 – 2006) strains of inactivated JE vaccine since 1988. Since 1st of July 2009, inactivated JE vaccine has been replaced by the live attenuated JE vaccine -SA 14-14-92 in the National Programme of Immunization.

## Indication:

Prevention of infections caused by JE virus and resulting deaths and disabilities.

## Schedule in Sri Lanka:

Due to likely interference with acquired maternal immunity during the first months of life, vaccination is not recommended before 6 months of age. In the National Programme, the vaccine is not given to children below one year of age. Children in the age group 1-10 years are eligible for vaccination. Primary immunization consists of two injections given at 1-4 weeks interval and the third dose given 1 year after the first 2 doses. the Booster Immunization dose is given generally every 4-5 years in order to maintain the effective immune level. Since there may be variations with individual commercial JE vaccine preparations, please refer to manufacturer's instructions for determining the exact timing for boosters of the vaccine

### Dose and administration:

Liquid vaccine is administered sub-cutaneously. For children under 3 years of age (1-3 years), the recommended dose is 0.25 ml. The recommended dose for those above 3 years of age is 0.5 ml. Liquid vaccine vials should be shaken well before being administered. Simultaneous administration of the inactivated JE vaccine with EPI vaccines such as measles, DPT and polio does not interfere with sero-conversion. However, the impact of co administration with non EPI vaccines has not been systematically studied.

### **Contra indications:**

Previous history of hypersensitivity to a dose of inactivated JE vaccine administered in an earlier occasion is the only contraindication for JE inactivated vaccine. However, following conditions and/or diseases have been listed as contraindications except when in the opinion of physicians withholding the vaccine entails even greater risk.

- 1. High fever or severe acute infection
- 2. Cardio vascular, renal or hepatic diseases
- 3. Diabetes
- 4. Severe malnutrition
- 5. History of convulsions or spasmodic symptoms within one year before vaccination
- 6. Leukemia, lymphoma and cancer in exacerbating phase Pregnancy

### **Adverse Events Following Immunization:**

Inactivated JE vaccine is generally considered safe. However, AEFI surveillance in Sri Lanka indicates that the reporting rate of AEFI for inactivated JE is the highest after that for DPT.

Results of AEFI surveillance data for inactivated JE vaccine in Sri Lanka is given in the table 9.

Table 9 : Distribution of reportedAEFI for the inactivated JEvaccine in Sri Lanka from 2003-2008

	2003	2004	2005	2006	2007	2008
Seizures	5	30	57	55	2	10
Allergic reactions	159	234	539	460	21	70
Abscess	0	10	10	6	0	1
Severe Local Reactions	3	5	34	48	9	0
High Fever (>38ºC)	38	69	183	157	7	45
Hypotonic Hypo-responsive episodes	0	0	0	0	0	1
Meningitis	0	1	0	3	0	0
Encephalitis	1	0	0	1	1	0
Guillan Barre Syndrome	0	5	0	0	0	1
Arthralgia	0	9	3	11	0	1
Persistant Screaming	0	0	0	0	0	2
Rate / 100000 doses	30.8	57.6	192.6	92.5	90.5	37.4

According to global data, local reactions such as swelling, tenderness and redness are reported in about 20% of vaccine recipients. A similar proportion of vaccinees have experienced, systemic reactions including headache, myalgia, gastro-intestinal symptoms and fever. Acute Disseminated Encephalomyelitis (ADEM) temporally coinciding with inactivated JE vaccine has been reported at frequencies ranging from 1 per 50000 to 1 per 100000 doses administered. However, according to the Global Advisory Committee on Vaccine Safety, ADEM is not a cause for concern when offering the vaccine as there is no increased risk of ADEM temporally associated with the inactivated JE vaccine. Occasionally, hypersensitive reactions such as severe urticaria, facial angio–oedema and respiratory distress have been reported, in particular, in vaccinees from non endemic areas. Practitioners need to remember that these reactions may occur as late as 12-72 hours following vaccination.

### Use in pregnancy:

Pregnant women should be vaccinated only when they are at high risk of exposure to infection.

### Usage of vaccine in specific circumstances:

For travellers aged more than one year visiting a JE endemic area for at least two weeks, current established practice is to administer 3 primary doses at days 0,7 and 28; alternatively 2 primary doses preferably 4 weeks apart. If continued protection is required, boosters should be given after one year and then every three years. Empirical evidence suggests that the inactivated JE vaccine can be used in different immunodeficiency status including HIV.

Forms of preparation : Both liquid and lyophilized vaccines

are available

Storage:

Lyophilized inactivated JE vaccine is stable at 4<sup>o</sup>C for at least one year. It should not be frozen nor should it be exposed to direct sunlight

## Live attenuated JE vaccine (LJEV) SA 14-14-2:

### Introduction

Manufacturing of LJEV is based on growth of the genetically stable, neuro-attenuated SA 14-14-2 strain of the JE virus on a mono layer of primary hamster kidney cells. After cultivation and harvest, an appropriate stabilizer is added to the virus suspension and then lyophilized. It elicits broad immunity against heterologous JE viruses with sufficient viral replication.

In 1988, the Chinese authorities licensed the LJEV SA 14-14-2 strain for use in China. Since then, it had been used to vaccinate more than 200 million children in China. Among other countries, India alone vaccinated nearly 30 million children in 2006 and 2007. Currently, more than 50 million doses of LJEV are produced annually in China. Other countries that have licensed and used the LJEV are South Korea (since 2001), Nepal (since 1999), and India (since 2006).

LJEV is produced in accordance with technical specifications in "Guidelines for the production and control of Japanese encephalitis vaccine (live) for human use" developed by the WHO Expert Committee on Biological Standardization. Although there are several producers of the Live JE vaccine in China, Chengdu Institute of Biological Products (CDIBP) is the only currently authorized manufacturer of the SA 14-14-2 vaccine for export.

### Indication:

Prevention of infections caused by JE virus and resulting deaths and disabilities

### Schedule in Sri Lanka

In Sri Lanka at the beginning of the JE immunization program with LJEV, Children were immunized with the LJEV at the completion of the first birthday (one year). However with the introduction of the MMR vaccine it has been decided to shift the age of immunization to 9 months. Though in certain other countries, a further booster dose is given one year after the primary immunization given at the completion of first birthday, many studies suggest that the immunogenicity given by a single dose is equivalent to that of when these two vaccines are given separately. Based on these data, a single dose is recommended to be used in Sri Lanka.

If due to any reason, the vaccine is missed or delayed on the due date, it should be given at the next earliest available opportunity for immunization. However if another live vaccine is to be given before or after this vaccine there should be a time gap of at least four weeks between the two vaccines.

## Dose

Vaccines

against J

Π

The recommended dosage is 0.5ml of reconstituted vaccine.

## Route and site of administration

LJEV should be administered <u>subcutaneously</u> to the outer mid thigh or upper arm depending on the age of the child.

## Contraindications

There are only a few contraindications for administration of live JE vaccine. General contraindications to vaccination specified in the Immunization Handbook issued by the Epidemiology Unit in 2002 are applicable to the LJEV as well.

However, It should be postponed in specific instances given below,

- Fever more than 38.5<sup>o</sup>C
- Acute stage of any infectious disease
- Temporarily acquired severe immunodeficiency states due to recent immuno suppressive therapy such as systemic corticos-teroids, chemotherapy, irradiation etc
- History of convulsion during the last 12 months

## It should be avoided in

- Children with proven or suspected hypersensitivity to LJEV or its components such as Kanamycin or Gentamycin.
- Congenital or acquired severe immunodeficiency states such as impaired immunological mechanisms, malignant conditions and Acquired Immuno Deficiency Syndrome etc

Please note that subjects with a previous history of moderate to severe allergic conditions (urticarea, dyspnoea, peri-oral oedema, laryngeal oedema) should be vaccinated in the central immunization clinic with an emergency tray and procedures for emergency care being ready.

## The following are NOT contraindications:

- Minor illnesses such as respiratory tract infection or diarrhea with temperature below  $38.5^{\circ}C(101^{\circ}C)$
- Family history of convulsions
- Treatment with topical corticosteroids or systemic use of corticosteroids at low dosages (less than 0.5mg/kg of prednisolone or equivalent) in case of skin diseases like dermatitis, eczema or other localized skin disorders
- Stable neurological conditions e.g. cerebral palsy, down syndrome.

## **Precautions:**

It is advised to review child's medical history before administration of the LJEV with a view to identifying children with compromised health status. Parents/ caregivers of such children should be communicated that there may be the possibility of coincidental worsening of the health status of the vaccinated child due to the compromised health status which could be erroneously attributed to the vaccination.

There should be a gap of at least four weeks between the live JE vaccine and another live vaccine administered before or after the live JE vaccine.

## Adverse Events Following Vaccination:

The general conclusion is that the LJEV SA14-14-2 is safe and even rare adverse events are extremely unlikely. Neither hypersensitive reactions nor encephalitis/ meningitis have been reported for the LJEV. Fever exceeding  $38^{\circ C}$  has been observed in about 10% of vaccine recipients whereas swelling and redness at the injection site is reported in less than 1%. Occasionally sporadic skin rashes which do not require treatment may appear.

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Results of AEFI surveillance data for live JE vaccine in Sri Lanka is given in the table 10.

Table : 10 Distribution of reported AEFI for the Live JE vaccine in Sri Lanka from 2009-2011 ( $1^{st}$  quarter)

		2009		2010	201	1 (1st Qtr)
AEFI	No.	Rate per 100,000 doses	No.	Rate per 100,000 doses	No.	Rate per 100,000 doses
Seizures	20	8	31	5.35	14	11.8
Allergic Reactions	172	68.8	379	65.4	85	72
Injection Site Absces	1	0.4	4	0.69	1	0.84
Severe Local Reactions	14	5.6	28	4.83	5	4.2
High Fever	56	22.4	137	23.66	17	14.4
Lymphadenitis	0	0	0	0	0	0
Encephalitis	0	0	1	0.17	0	0
Meningitis	0	0	1	0.17	0	0
Nodule	0	0	7	1.2	0	0
Arthargia	9	3.6	1	0.17	0	0
Encephalopathy	0	0	1	0.17	0	0
Persistant Screaming	1	0.4	1	0.17	0	0
Toxic Shock Syndrome	0	0	0	0	0	0
Others	9	3.6	80	13.8	7	5.9
HHE	2	0.8	3	0.51	1	0.84
Injection Reaction	1	0.4	0	0	0	0
Total	285	114	674	116.4	130	110

### Forms of preparation:

LJEV is a lyophilized powder which turns into a transparent orange red liquid after reconstitution.

## Storage:

LJEV should be stored in a temperature between  $2-8^{\circ}$  C and protected from sun light. The vaccine should not be frozen. If the vaccine is not used immediately after reconstitution, it should be stored at 2°C to 8°C not longer than 2 hours and away from light. After 2 hours it should be discarded.

## Use in pregnancy:

LJEV is contraindicated for pregnant women. However, if vaccine is required in pregnancy, it is advisable to administer inactivated JE vaccine. Physician should asses the risk benefit of recommending the vaccine to pregnant woman

## **References**

- 1. Rao PN. Japanese encephalitis. Indian Paediatrics 2001;38:1252-1264
- Rao PN. Japanese encephalitis In : Frontiers in Paediatric Neurology, Vol V. Common Paediatric Neurological Problems, October 2001. Ed. Rao PN. Hyderabad, Neuroped Publication 2001; pp1-70
- Burke DS, Nisalak A. Detection of Japanese encephalitis virus Immunoglobulin M antibodies in serum by antibody capture radio-immunoassay. Journal of Clinical Microbiology 1982;15:353-361
- Schwartz E, Mileguir F, Grossman Z, Mendelson E. Evaluation of ELISA-based sero-diagnosis of dengue fever in travelers. Journal of Clinical Virology 2000;19:169-173
- 5. Laboratory Manual, Microbiology. 2001 Produced by Sri Lanka College of Microbiologists. Ed. Thevanesam V.
- A Handbook on Collection and Transport of Specimens for Microbiological Investigations (2001), Sirimali FernandoPATH. Japanese Encephalitis project . Available from <u>http://</u> www.path.org/projects/JE in depth.php
- 7. World Health Organization (2006). Japanese Encephalitis (position paper).
- 8. Weekly Epidemiological Record. (81), 331-40. Epidemiology Unit (2009). Guidelines for introduction of live Japanese encephalitis vaccine SA 14-14-2 in Sri Lanka.
- 9. Epidemiology Unit (2000). Immunization hand book. pp 82-86.
- 10. World Health Organization (2002). Guidelines for the production and control of Japanese encephalitis vaccine (live) for human case. Technical Report Series, No 910. pp 66-98
- 11. World Health Organization (1988). Requirement for Japanese Encephalitis vaccine (inactivated) for human use. Technical Report Series, No 771, pp 133-157.
- 12. World Health Organization. Manual for the laboratory diagnosis of Japanese Encephalitis Virus Infection 2007
- 13. World Health Organization. Japanese Encephalitis surveillance standards. 2006

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## Annexure 2

#### சைலிகம் / ககாதாரம் / Health - 544

### வேச்சேல் கேர்க் குதுக்கு குதுக்கு தோற்றுநோய் பற்றிய அறிவிப்பு NOTIFICATION OF A COMMUNICABLE DISEASE

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## Annexure 1

Annexure 3



සැලකිය යුතුයි.—(1) 5, 7, 10, සහ 11 කරුණු අදාල කොටුවේ × ගැසීමෙන් සම්පූර්ණ කළ යුතුයි. අනිකුත් කරුණු සලකා ඇති ඉඩ පුමාණයයෙහි සටහන් කළ යුතුයි. කායබාලීය පුයෝජන සඳහා වෙන් කර ඇති කොටුවේ කිසියම සටහනක් නොකරන්න.

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Notes.-(1) Items 5.7,10 and 11 should be completed by placing a × in the appropriate box. Other items should be entered in the space provided. Plese do bot enter anything in space for office use. (2) Items 9 should be completed in as much details a possible, e.g., "Paratyphoid A" and NOT "Enteric fever"

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## Annexure 4





## Annexure 5

EPID/DS/JE/2010

SURVEILLANCE OF ENCEPHALITIS - CASE INVESTIGATION FORM EPIDEMIOLOGY UNIT, MINISTRY OF HEALTH

Investigation should necessarily be carried out by the MOH/AMOH and under no circumstances it should be done by the PHI. Nor should the investigation form carry a signature of any other officer than the MOH or AMOH. (GS 01/42/2008)

Week Ending:

2. Residential Address: ....

4. Age	5. Sex 1. Male 2. Female	6. Ethnic group	7. Occupation	8. DPDHS Division	9. MOH area	
	9. Unknown 3. Moor 4. Others 9. Unknown	3. Moor	FOR OFFICE USE ONLY			
		9. Unknown				

B. PRESENT ILLNESS/OUTCOME

10. Date of onset of symptoms:	12. Was patient admitted to hospital	17. Date of discharge/ transfer or death:
dd mm yy	2. no _ skip .	d d mm y y
11. Where did the patient first seek medical advice ?	3. not known 5 to Q.21	18. If transferred to, name of hospital
1. government hospital     2. private hospital	13. If yes, date of admission	19. Was patient transferred from some other hospital?
3. private practitioner     4. Ayurvedic institution     (public/private)     5. other (specify)	14. Name of hospital: 	20. If 'yes', where was the patient transferred from?
	16. BHT No:	21(a). Outcome of the case 1. cured 3. transferred 2. died 4. not known
		21(b). If "Cured", was there Neuro- Psychiatric sequalae 1. Yes 2. No If "Yes" Please Specify

#### C. CLINICAL DATA

Case definition : an illness with acute onset of possible meningitis / encephalitis including high fever and altered mental status

22. Symptoms and signs

a. general	b. mental state and other neurological symptoms and signs	For office use only
high fever headache nausea/vomiting abdominal pain loose motion	unconscious droway (abnormally sleepy) coma lethargic irritable abnormal behaviour / movements convulsions	Laboratory case definition Probable Viral Encephalitis 5-1000 cella/mm3 in CSF (predominantly lymphocyte) Confirmed encephalita due to JE virae Presence of JE ant IgM in CSF/sen OR Rising thre of JE ant IgM in pain sens.
	focal neurological     tremors     meningeal signs (neck stiffness/Kerning's sign)     others (specify):	Compatible with the case definition