

INVESTIGATION OF A SUSPECTED OUTBREAK OF JAPANESE ENCEPHALITIS IN PULAU LANGKAWI

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Summary

An investigation was carried out on a suspected outbreak of Japanese encephalitis (JE) during the month of June 1979 in Pulau Langkawi, in the state of Kedah, Malaysia.

Results incorporating the clinical features, laboratory and serologic findings, and brief epidemiological survey showed 60% of the cases to be positive for JE infection. Another 20% were suggestive of JE, but diagnosis could not be confirmed as death had occurred prior to the start of the investigation.

The outbreak appeared to be localized in 2 areas in Langkawi, and 90% of the cases affected were between the ages 5-15.

The mosquito vectors for JE were shown to be present in Langkawi, but the 'link' host between the normal animal cycle and man could not be determined. No virus isolation was attempted.

INTRODUCTION

Japanese encephalitis (JE) virus is common over a wide part of Asia. It has been reported in areas ranging from southern India to parts of S.E. Asia, and through to Japan and the islands in the Pacific.^{1,2} The distribution of JE can be broadly categorized into 2 main regions - the areas in which JE epidemics are a serious and regular occurrence; and the regions in which JE is believed to be endemic.³ The former include Japan, Taiwan and Korea^{2,4,5} while countries included in the latter are Malaysia, south-east India and parts of Thailand.⁶⁻⁸

The virus is transmitted by several closely related species of *Culex* mosquitoes among the wild vertebrate hosts. Evidence available indicates that the normal enzootic cycle of JE is a wild-bird/mosquito cycle and that mammals usually serve as dead-end hosts in the cycle.² The link between the natural cycle and the establishment of epidemics in man is believed to be via animals. Several workers, for example, have shown the pig to aid in the transmission of JE to man?¹⁰

In Malaya, Cruickshank,¹¹ in a retrospective study, attempted to show the existence of JE among British prisoners of war during the Japanese occupation. The study was based on clinical reports only, and hence it could only be speculated that the symptoms studied were

caused by a Japanese encephalitis virus. In 1951, however, an outbreak of equine encephalitis among imported race horses, followed closely by a fatal case of human encephalitis, was reported¹² and later confirmed to be JE. Subsequent work has demonstrated the existence of the virus in Peninsular Malaysia and Sarawak.^{6,13-16} The disease has been monitored by the United States Army Medical Research Team and the Institute for Medical Research, Kuala Lumpur; and the figures available indicate an endemic level of infection (Table 1).

As can be seen from Table 1, the incidence of JE is low and fairly evenly distributed throughout the year. Hence, when 9 cases of suspected JE were reported to the Institute for Medical Research in July, it was decided to investigate this probable outbreak.

MATERIALS AND METHODS

Subjects

The 9 reported cases were all from Pulau Langkawi which had been referred by the district hospital there to the general hospitals at Kangar, Perlis and Alor Star, Kedah.

Of these 9 cases, 2 were excluded from the study as bacterial meningitis and bronchopneumonia were shown to be the cause of disease.

Further investigation revealed 3 additional

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TABLE 1
DISTRIBUTION OF LABORATORY CONFIRMED JE CASES
BY MONTH BETWEEN 1974-1978

Figures obtained from the Institute for Medical Research¹⁷

<i>MONTHS</i>	<i>1974</i>	<i>1975</i>	<i>1976</i>	<i>1977</i>	<i>1978</i>
January	1	1	—	—	2
February	3	3	—	—	1
March	1	4	2	—	1
April	4	—	4	—	—
May	2	2	1	—	—
June	1	2	2	—	—
July	—	5	4	1	—
August	1	—	—	1	4
September	1	2	—	2	2
October	1	1	3	2	2
November	1	2	3	—	2
December	3	1	—	4	2
TOTAL:	19	23	19	10	16

cases with possible JE symptoms, making the number of cases studied to 10.

Langkawi (with ref. to Fig. 1)

The Langkawi group of 99 islands is situated 30 kilometers west of Kuala Perlis, Perlis, at the northern tip of Peninsular Malaysia. The majority of the islands are uninhabited with the exception of a few like Pulau Tuba. The largest island in the group is Pulau Langkawi on which the majority of the population is concentrated.

The population in Pulau Langkawi is mainly rural, with only one main urban center – the town of Kuah with a population of just over 2,000. The main occupations are fishing and rice cultivation. Some rubber cultivation is also carried out.

Study Design

The investigation was divided into two main parts: a diagnostic review based on the clinical features and serologic investigations; and a brief epidemiological survey.

Clinical Criteria

Patients who satisfied the following criteria were included in the study:

- (i) They had been clinically diagnosed as encephalitis, meningitis or meningo-encephalites.¹⁸

and (ii) Their illnesses fell between the months of May and June 1979.

Of the cases included in the study, there were 2 deaths prior to the start of the investigation. No post-mortem had been carried out, and hence, no brain specimens were available for study.

Serologic Criteria

The diagnosis of JE was serologically determined using the microtitre Haemagglutination-Inhibition (HI) test.^{9,20} Eight units of each haemagglutinating antigen were used in the simultaneous testing for JE, Dengue 1, Dengue 2, Dengue 3, Dengue 4, Tembusu, Zika and Sindbis antibodies.

Of the 10 cases, serologic tests were not carried in two instances as the patients had died prior to the arrival of the team and no blood specimen had been taken.

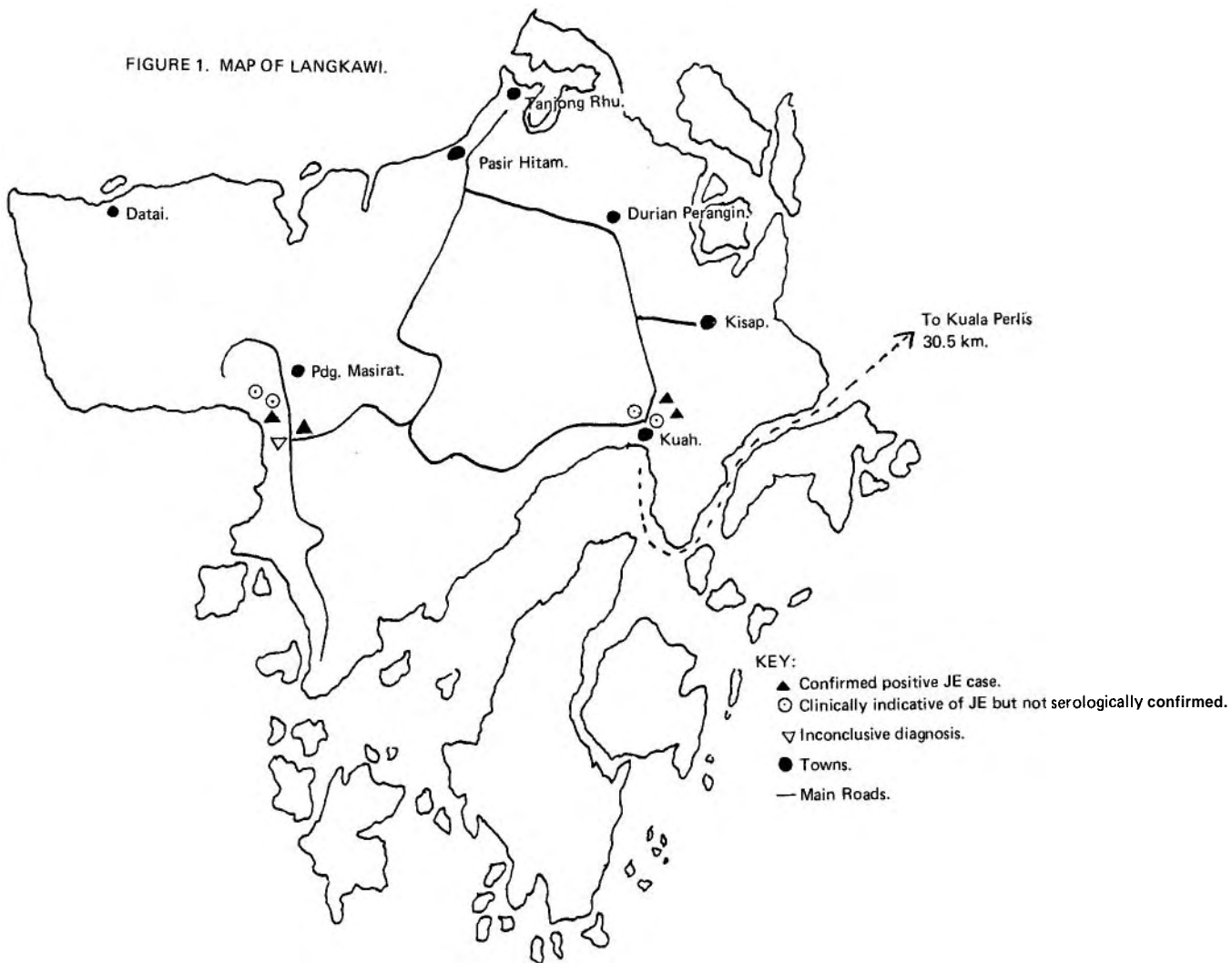
No virus isolation was attempted due to the lack of facilities on the island.

Epidemiological Survey

The survey consisted of investigations of the patients' household and surroundings.

Note was taken of the sex-age distribution of the patients. Other factors considered included determining the movements of the patients prior to the onset of the disease and whether

FIGURE 1. MAP OF LANGKAWI.



any member of the house-hold had been ill prior to, during or subsequent to the patient's illness.

The animals reared or present in the immediate vicinity of the household were also noted. Particular attention was paid to determine if there was a 'link' or amplifier host present. For example, an attempt was made to bleed water buffaloes to see if residual JE antibodies were present, as no pigs were observed due to the community being almost entirely Muslim.

The investigators also attempted to determine the different mosquito species present in the area.

RESULTS

Clinical Evaluations

Signs and Symptoms:

The clinical manifestations of the 10 cases are summarised in Table 2. The onset and course of the illness were similar to that reported in the series of JE studies around this region.^{4,21-23} All cases (100%) presented with an acute onset of high fever; 50% of which were above 104°F after admission. Other presenting symptoms were headache (90%), nausea and vomiting (70%) and convulsions (60%). There was cloudiness of the sensorium and shortly after admission, all cases became drowsy or comatose. 40% had upper respiratory tract complaints. The average duration of illness before hospital-

isation was 3.2 days, reflecting upon the acuteness of the illness.

There was some difficulty in evaluating the physical signs due to the impairment of sensorium. However, based on the studies of case records, 70% showed signs of meningeal irritation (nuchal rigidity and Kernig's sign), 20% showed pupillary changes (pupil constriction). One case showed a mild papilloedema on (L) fundus. 20% had extensor planter response. 50% of them developed hemiplegia during the course of the disease, most of them recovered subsequently (see below). 2 cases developed aphasia.

Sequelae

Out of the 2 reported deaths, one case died on the 6th day of illness (3rd day of hospitalisation). The other case died on 13th day of illness at home, after the patient was discharged at own risk (AOR) about one week earlier.

Apart from the 2 deaths, one case was still critically ill at the time this study was done. The patient was in deep coma, with spasticity of all 4 limbs, right conjugate gaze and brisk reflexes with extensor plantar. The remaining cases regained their consciousness. The majority of them were discharged between 9th-18th day of hospitalisation. One case however has a residue (R) sided hemiparesis. Another case was mentally retarded after the illness.

TABLE 2
CLINICAL MANIFESTATIONS OF 10 CASES OF ENCEPHALITIS STUDIED

<i>Clinical Manifestations</i>	<i>No. of Cases</i>	<i>% of total</i>
Fever	10	100%
Headaches	9	90%
Arthralgia/myalgia	1	10%
Cough/rhinitis	4	40%
Nausea or vomiting	7	70%
Drowsiness or coma	10	100%
Convulsions	6	60%
Paralysis	5	50%
Meningeal signs	7	70%
Pupil changes	2	20%
Papilloedema	1	10%
Extensor Plantar	2	20%
Aphasia	2	20%

Laboratory investigations:

The average white blood cell count was 8,580/cu millimeter, and ranged from 6,300 to 18,100. None of the cases showed any significant alteration in differential count.

Lumbar puncture was done in 7 of the 10 patients. Two cases had a normal picture on microscopic and biochemical examination. The cerebral spinal fluid was clear in all cases. Three patients had a cell counts of more than 100, with lymphocytes ranging from 50–90%. CSF proteins were raised in 2 patients (above 45 gm %). Sugar levels was normal in all cases. Gram staining, AFB staining and Indian Ink staining were negative in all cases.

Serologic Results

From the serologic results, 4 cases were shown to be positive to Group B Arbovirus (Flavivirus) infections, while the remainder did not show any significant rise in titre.

A positive result was accepted when a four-fold rise in titre was obtained from paired sera in a clinically diagnosed case.

Epidemiological Findings

The age and sex distributions of the patients are shown in Table 3. Two cases were below 5 years old; 2 cases between 6–10 years old; 3 patients were between 11–20 years, while the remainder were over 20 years. The majority of the cases (80%) were male.

The survey also showed that the cases were all confined to the main island of Pulau Langkawi. The one patient whose address was given as Pulau Tuba was shown to have contacted the disease while studying at the residential school

in Pulau Langkawi. No other reported cases came from Pulau Tuba, and inquiries among the villagers there did not reveal any further cases with encephalitic symptoms.

The cases were from two main areas – the villages around the town of Kuah, and the area around Padang Masirat (Fig. 1).

These two localities were low-lying with extensive rice fields in close proximity. In the vicinity of Kuah, rubber and coconut plantations were also present. The houses were of wood and palm-thatch construction, with many raised on stilts. The surroundings of the houses visited were generally well kept, and the houses were built on sandy ground.

The animals common to all the houses were water buffaloes, chickens, ducks, cats and dogs. The attempt to bleed water buffaloes was unsuccessful, as the co-operation of the villagers was not obtained.

The survey also revealed that no other members of the respective household had been ill prior to or during the period of illness. The disease was also of local origin as none of the patients or their families had travelled to the mainland in the month preceding the onset of disease. There appeared to be no additional unreported cases with JE symptoms, although reference was made to one case who had died during the month of June. This particular patient was included in the survey because he had presented with symptoms suggestive of encephalitis. He had been discharged AOR and had subsequently died at home. This particular case lived in the vicinity of Padang Masirat, and was only several houses away from another reported case.

TABLE 3
AGE AND SEX DISTRIBUTION

Age Group	No. of Cases	Sex Distribution	
		Male	Female
0 – 5	2	2	0
6 – 10	2	1	1
11 – 20	3	2	1
21 – 40	2	2	0
40 and above	1	1	0
TOTAL	10	8	2

The numbers and various species of mosquitoes caught are given in Table 4. The main vectors for JE virus – *C. tritaeniorhynchus* and *C. pseudovishnui*, were present in the area of confirmed JE. The numbers of mosquitoes trapped were small, but this could have been due to the several consecutive days of heavy rainfall prior to the investigation, and also to the fact that the staff of the Health Department had carried out extensive fogging (Reslin in diesel) operations as a preventative measure.

DISCUSSION

The outbreak in Pulau Langkawi can be concluded as JE based on the clinical comparability of the cases with JE, the serologic findings and the presence of the probable vector mosquitoes.

The 'link' or amplifier host in the transfer of the disease to man was not established during this investigation. The usual host-the pig – was absent on the island. Of the animals present in Langkawi, the most common was the water buffalo. However, several workers^{24, 26} have suggested that the buffalo, and bovines in general, are not important amplifying hosts for JE and may even act in suppressing JE infec-

tion. It was, however, not possible to determine if this was the case in Pulau Langkawi as the villagers did not permit the water buffaloes to be bled for serologic examination. The other domestic animals present – chickens, ducks, cats and dogs – have not been previously implicated as hosts; although both Pond³ and Simpson¹⁵ have demonstrated serologic evidence of JE infection in dogs.

Results of the HI tests showed a characteristic rising titre indicative of a primary JE infection. There were two clinically diagnosed cases of JE whose HI results failed to show a characteristic rise in titre. This may be explained by the fact that the first sera were only collected approximately 2 weeks after the onset of disease. As the characteristic rising titre is usually only demonstrable within the first week of infection, it is possible that in these two cases the HI test would be inconclusive.

This particular outbreak was confined mainly to children, as 90% of the confirmed cases were between the ages of 5–15 years. The majority of those affected were also males, thereby suggesting a possible sex-related susceptibility to JE. However, several workers^{23, 25}

TABLE 4
MOSQUITO SPECIES AND NUMBERS CAUGHT ON
PULAU LANGKAWI

*Indicates possible vector species for JE^{2,4}

Mosquito Species	No. Caught
<i>Culex annulus</i> *	26
<i>bitaeniorhynchus</i>	4
<i>fuscocephalus</i> *	4
<i>pseudovishnui</i>	3
<i>sinensis</i>	13
<i>sitiens</i>	7
<i>tritaeniorhynchus</i> •	15
<i>Aedes albopictus</i>	8
<i>Armigeres subalbatus</i>	1
<i>Anopheles barbirostris</i>	1
<i>korwari</i>	4
<i>philippenensis</i>	28
<i>vagus</i>	4

²⁹ have not shown this to be the case. Grossman³⁰ has suggested that the reason for the higher incidence of clinical illness in males was because males were more likely to be outside late in the evening and hence be exposed to JE virus-infected mosquitoes.

The incidence of disease among children is similar to the outbreaks in Korea and Taiwan where JE is almost entirely a disease of young children⁵ and also in Singapore.^{23,31} Figures available from the Institute for Medical Research for the years 1970–1978 show that the age group mainly affected is between 5–14 years, thus showing this outbreak to be similar in pattern. The only difference was that in this instance, the children affected were all Malay in origin; whereas the cases for the past 8 years in Malaysia show a higher incidence rate among the Chinese population. This may be due in part to the fact that Pulau Langkawi is basically a rural area with a predominantly Malay population. Paul³¹ has stated that the disease appears to be more marked in rural areas in Singapore as a result of the high mosquito population and pig-breeding. However, this would not necessarily apply to Pulau Langkawi where the population is almost entirely Muslim and hence there is no pig rearing. It would be of interest, therefore, if further studies were to be carried out in order to determine the reservoir host in Pulau Langkawi.

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