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Short communication

A decade of Japanese encephalitis surveillance in Sarawak, Malaysia: 1997–2006

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Summary Japanese encephalitis virus (JEV) is an important encephalitis virus in Asia, but there are few data on Malaysia. A hospital-based surveillance system for Japanese encephalitis (JE) has been in operation in Sarawak, Malaysia, for the last 10 years. JEV is endemic in Sarawak, with cases occurring throughout the year and a seasonal peak in the last quarter (one-way ANOVA, $P < 0.0001$). Ninety-two per cent of 133 cases were children aged 12 years or younger; the introduction of JE vaccination in July 2001 reduced the number of JE cases (84 in the four seasons prior to *vs*. 49 in the six seasons after, McNemar's test, $P = 0.0001$). After implementation of the programme, the mean age of infected children increased from 6.3 to 8.0 years (Student's *t*-test, $P = 0.0037$), suggesting the need for a catch-up programme.

keywords Japanese encephalitis, surveillance, vaccine

Japanese encephalitis virus (JEV), family Flaviviridae, is the type species of the Japanese encephalitis serological group of flaviviruses that includes West Nile virus. JEV is transmitted by *Culex* spp. mosquitoes and is maintained in a vertebrate host–mosquito cycle where pigs and water birds are the main amplifying hosts and humans merely incidental hosts. JEV is considered the most important cause of encephalitis in Asia with 30 000–50 000 cases reported annually. Most infected individuals are asymptomatic but of those who do present with encephalitis, 25–30% of cases are fatal while half of the survivors have severe neurological sequelae (Solomon *et al.* 2000; Mackenzie *et al.* 2004). The disease burden associated with JEV is not well appreciated and it has only been in the past few years that the importance of JE has been brought to general attention with the recognition of large outbreaks of JE in parts of India and Nepal. Even in countries where it is assumed that JE does not occur, such as Indonesia, a recent hospital-based surveillance study in Bali has shown that JE incidence and case-fatality rates are similar to those of other JE endemic countries (Kari *et al.* 2006).

In Malaysia, there is a paucity of data on JE. Two outbreaks have been recorded in the literature – Pulau Langkawi in 1974 (Fang *et al.* 1980) and Penang in 1988 (Cardosa *et al.* 1995). A series of studies from the 1960s documented JEV isolation from mosquitoes in Sarawak and showed that pigs play an important role as amplifying hosts (Bendell 1970; Simpson *et al.* 1970, 1974, 1976; Bowen *et al.* 1975). Seroconversion to JEV in pigs suggested that transmission occurs throughout the year with infection rates higher in the period from November to January coinciding with the major seasonal population increase of *Culex tritaeniorynchus* (Simpson *et al.* 1976).

In 1997, a pilot hospital-based surveillance study for JE was set up in Sibu Hospital in Sarawak, followed in 1998 by passive surveillance for all other hospitals in the state. Patients were suspected to have Japanese encephalitis if they had fever (or a history of fever), and at least one of the following: reduced level of consciousness (lethargy, drowsiness or coma); severe headache; neck stiffness; tense anterior fontanelle; focal neurological signs and prolonged seizures.

Paired sera and paired CSF for each patient were considered to be the ideal specimen set. However, in reality the complete specimen set was not obtained from many cases. Specimens were tested for JEV specific IgM by MAC ELISA (Venture Technologies Sdn Bhd, Malaysia), which distinguishes IgM elicited by JEV from that elicited by dengue viruses (Solomon *et al.* 1998; Cardosa *et al.* 2002).

The sensitivity, specificity, positive predictive value and negative predictive value of the test used were 83%, 99%, 0.98 and 0.92, respectively for CSF and 91%, 95%, 0.92 and 0.94, respectively for serum.

All cases of encephalitis with specific IgM to JEV in serum and/or CSF were considered to have been infected recently with JEV. It should be noted that patients with single IgM-negative sera or CSF cannot be considered conclusively negative because an IgM seroconversion can occur in a second specimen. With only single specimens, we lose this information. Here we report data obtained over a 10-year period from 1997 to 2006. Four seasons into the study period, in July 2001 the Sarawak Health Department implemented a JE vaccination programme. JE vaccine (Biken, Japan) was included in the Expanded Programme of Immunization (EPI), covering children aged 1–2 years. All individuals aged 1–15 years in the household of every identified JE case were also vaccinated. There are some cultural factors that are notable in our practice of vaccination of case contacts. Many rural communities in Sarawak live in longhouses. These are single structures that house many individual family units with a common connecting veranda called *ruai*. Thus there is very close contact and frequent movement of people among different families in our longhouse villages. In our control programme we have treated each longhouse as a single household.

A total of 133 patients with serologically confirmed recent JEV infection were admitted into Sibu Hospital during the study period. One hundred and twenty-two (92%) were children aged 12 years and younger, 11 (8%) patients were older children and adults. After the introduction of JE vaccination in Sarawak, we recorded a reduction in JE admissions (Figure 1) in Sibu Hospital: 84 (63%, 79 children aged ≤12 years, five adults) of 133 patients between the months of February 1997 and June 2001 (Table 1), compared with 49 (37%, 43 children ≤12 years, six adults) of 133 patients were hospitalized between the months of July 2001 and December 2006 (McNemar's test, $P = 0.0001$). We also observed an increase in the age of affected patients. The mean age (range) of all affected patients shifted from 7.0 (0.3–28) to 9.2 (1.3–27.4) years (Student's *t*-test, $P = 0.0066$). Further subgroup analysis for children ≤12 years showed that the mean age of affected under-twelves increased from 6.3 (0.3–12) to 8.0 (1.3–12) years (Student's *t*-test, $P = 0.0037$). This shift in age distribution has also occurred in other countries where JE vaccine was introduced, namely in Japan, Korea, China and Taiwan (Tsai *et al.* 1999).

Our data show that JE is seasonal in Sibu with a significantly higher number of cases in the last quarter of each year, and sporadic cases throughout the year. It confirms the conclusion of the pig seroconversion study in the early 1960s suggesting that there is higher rate of transmission of JEV during the period of November to January (Simpson *et al.* 1976).

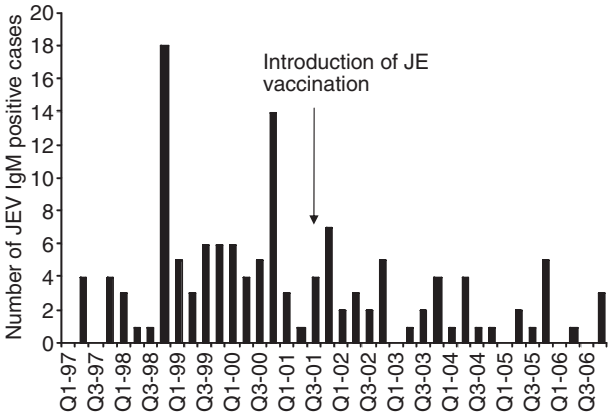

Figure 1 Japanese encephalitis (JE) admissions in Sibu Hospital between 1997 and 2006. The bars represent the number of JE admissions in Sibu Hospital by quarter of the year over the 10-year study period, 1997–2006 (Q1 = January–March, Q2 = April–June, Q3 = July–September, Q4 = October–December).

Table 1 Cumulative distribution of JE cases presenting to Sibu Hospital by quarter of the years 1997–2006

Quarter	Mean	Standard deviation	Standard error	Range	Cumulative total
Q1	3.6	5.8	1.8	0–20	20
Q2	4.4	6.6	2.0	1–24	24
Q3	4.0	6.3	1.9	0–22	22
Q4	12.2	18.9	5.7	1–67	67

Our focus on a single hospital in the state allowed us to be more certain of the true numbers of cases being seen at this hospital and has given us a clear picture of the trends in JEV infection in Sarawak. We believe that despitehe fact that the numbers of cases notified throughout the state are likely to be an underestimate of the true incidence of JE in Sarawak, obtaining accurate data from a major hospital in the state will allow some measure of confidence in providing an evidence base from which to make decisions about public health interventions.

We had an opportunity to obtain a better estimate of the numbers of JE cases in Sarawak during the season of 1998/1999 when there was a large outbreak of fatal viral encephalitis in Peninsular Malaysia (Chua *et al.* 1999; Farrar 1999). This outbreak, of the newly discovered

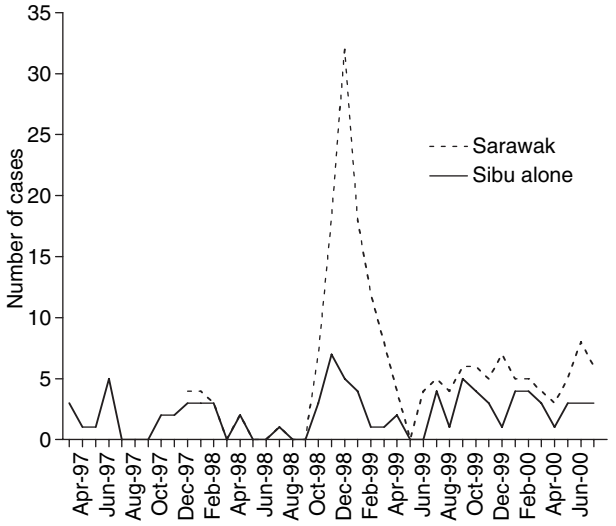

Figure 2 Comparison of Japanese encephalitis (JE) cases from Sibu Hospital and the State of Sarawak. The solid line represents numbers of JE cases from Sibu Hospital and the dotted line represents numbers of cases from the whole state of Sarawak, inclusive of Sibu Hospital.

Nipah virus (Lam & Chua 2002), was originally misdiagnosed as being due to JEV. Doctors in all hospitals in Malaysia were reminded to notify encephalitis cases to the public health authorities and we thus had an unusually high number of cases of encephalitis with specimens submitted to the laboratory. Figure 2 shows that during this season of 1998/1999, there was a large increase of cases reported in the state suggesting that JE is probably under reported most years.

In conclusion, we report that the introduction of the Biken JE vaccine in Sarawak has reduced the incidence of the disease. The total population of Sibu is 600 000 with 180 000 under 12 years of age. The data we have obtained over this last decade of surveillance show that the average annual incidence of JEV was 9.8 per 100 000 population under 12 years, dropping to 4.3 per 100 000 population under 12 years after the introduction of JE vaccination.

The policy of vaccinating 1 to 15-year-old household contacts of JE cases immediately probably contributed to the remarkable reduction in the JE caseload after the introduction of the vaccine. We introduced this practice because of specific cultural factors, especially because of the longhouse mode of living common among our rural communities, with animals reared under or near the longhouse. However, because we did not have a programme of 'catch-up' vaccination for the general paediatric population, we have seen a shift in the age of JE cases to older children and teenagers.

Another point to note is that JEV is a zoonotic virus and humans are incidental and dead end hosts. Thus any vaccination programme would have to target all susceptible individuals without expecting herd immunity to contribute to a reduction in incidence. For these reasons, the implementation of JE vaccination into any JE endemic area should take into consideration the need for a 'catch-up' immunization programme at the time of introduction of vaccine into the routine EPI.

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