

## Medicine in the Tropics

# Japanese encephalitis – an important cause of acute childhood encephalopathy in Lucknow, India

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**Summary:** Eighty-six randomly selected children between 6 months and 12 years of age admitted with acute unexplained encephalopathy over a one year period were examined for evidence of Japanese encephalitis. One or more indicators of the infection were present in 36 (41.8%). Viral isolation from brain tissue was possible in 2 of 12 patients and from cerebrospinal fluid in 19 out of 62 patients. Serological evidence of probable Japanese encephalitis was found in 21 out of 36 patients. Japanese encephalitis is an important cause of acute childhood encephalopathy in the Lucknow area, where it is probably endemic.

### Introduction

Acute encephalopathic illness constitutes an important cause of hospital admissions and deaths in children in India.<sup>1</sup> Causes of acute encephalopathy are varied and include bacterial and viral infections of the central nervous system, cerebral malaria, Reye's syndrome, poisoning and electrolyte disorders and many others. Often, no definite cause can be assigned and a presumptive diagnosis of 'viral encephalitis' is made. Epidemics of viral encephalitis have been reported from various parts of India including Uttar Pradesh in the past.<sup>2–4</sup> There remains, however, a need for systematic round the year studies on the aetiology of acute encephalopathic illness seen in children in India.<sup>1</sup> The present study is part of an ongoing project on acute encephalopathies in children. This communication is a report on some preliminary findings relating to the role of Japanese encephalitis.

### Patients and methods

Consecutive patients with acute encephalopathic illness (acute, nontransient alteration of consciousness with or without fever or other neurological symptoms) were taken for study if their age was between 6 months and 12 years and the

duration of the illness on admission was less than 1 week. Patients presenting to this hospital are mostly from the lower socio-economic class from both rural and urban areas of Lucknow and surrounding districts.

A proforma directed history was taken and examination performed on admission. A careful record of the patient's progress in hospital was maintained. An attempt was made to determine the cause of the illness by blood chemistry, blood culture, peripheral smears for malarial parasite, cerebrospinal fluid (CSF) examination and other relevant investigations. Samples for virological investigations were taken in all those cases in which the cause of the illness could not be otherwise established. Of these, 86 cases were randomly chosen by the laboratory for investigation. These cases were taken without referring to the clinical features of the case. Representative samples from all the months of the year were included.

### *Virological methods*

The following samples were collected for the diagnosis of Japanese encephalitis: (1) cerebrospinal fluid (CSF); (2) acute and convalescent phase sera (taken at least 10 days apart); (3) post-mortem brain biopsy, whenever possible. This was taken in minimum essential medium without serum.

All samples were immediately kept at 4°C and transported in ice to the Virology Laboratory of the King George's Medical College, Lucknow,

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which is one of the reference laboratories for Japanese encephalitis in India, within 24 hours. Here they were kept at  $-20^{\circ}\text{C}$  until tested.

Isolation of virus from brain tissue and CSF was done by intracerebral inoculation into 1–2 day old mice.<sup>4</sup> Identification of the virus was done by the Quick complement fixation test<sup>5</sup> using the brain suspension of sick mice as a crude antigen against hyperimmune sera of Dengue virus serotypes 1, 2, 3, 4, Japanese encephalitis, West Nile and Chikangunya viruses. The sera were obtained from the National Institute of Virology, Pune.

Haemagglutination inhibition test was performed on acute and convalescent phase sera using the microtitre technique.<sup>6,7</sup> A 4-fold or more rise in antibody against Japanese encephalitis virus (JEV) was taken as evidence of probable JEV infection.

**Results**

Over a 1 year period from 1st November, 1985 to 31st October, 1986, a total of 187 cases of acute unexplained encephalopathy were enrolled. Virological investigations were done in 110 samples from 86 patients. JEV was isolated in 2 of 12 brain biopsies and 19 out of 62 CSF samples. Serological evidence of JEV infection was found in 21 out of 36 cases tested. A total of 36 cases out of 86 (41.8%) had evidence of JEV infection. Of these 36 cases, 24 (66.6%) were of rural origin. The monthwise distribution of the cases (Figure 1) shows that although the disease was seen all through the year, a slightly larger number of cases occurred between September and November which

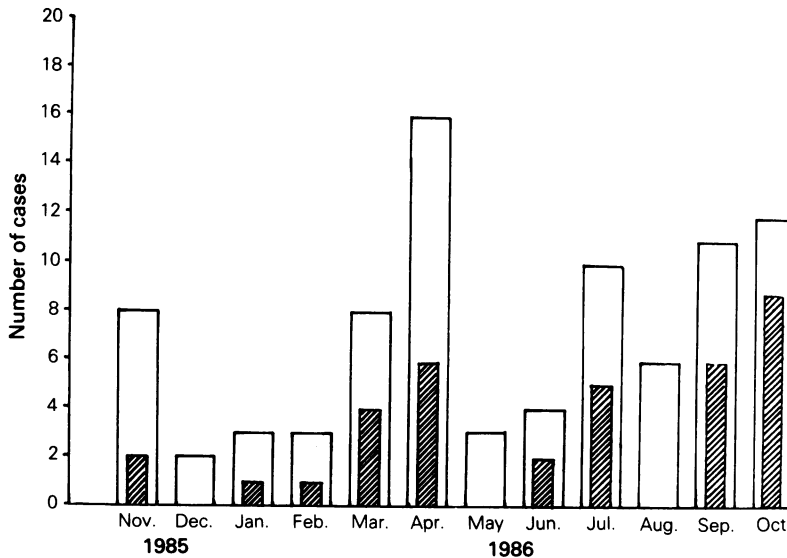
is the post-monsoon season and coincides with the period of peak mosquito prevalence. Sixteen (44.4%) of the patients died while in hospital.

**Discussion**

Since the mid-fifties JEV activity has been noted in various parts of India, both in the form of outbreaks of encephalitis<sup>2-4</sup> and the level of antibodies found in the population.<sup>8,9</sup> In contrast there are only a few reports on the sporadic occurrence of Japanese or other arboviral encephalitides.<sup>10</sup> This is the first large, comprehensive, prospective study on the year-round occurrence of Japanese encephalitis from Northern India in which all the cases had laboratory evidence of the infection.

The patients examined in this study were taken at random from all the cases of acute unexplained encephalopathy enrolled over a 1 year period. As consecutive cases presenting within a week of the onset of the illness were enrolled, our patients were unselected. Infants below the age of 6 months were excluded from the study, because young babies often present with depression of the sensorium even with non-neurological disorders.

In this study, it was observed that of 86 children with acute encephalopathy examined 36 had one or more indicator of JEV infection to suggest that this was the probable cause of the illness in these cases. This high number indicates that JEV is an important cause of acute encephalopathic illness in children in this area. The cause of the illness in the remaining 50 cases is still undefined. It is not



**Figure 1** Monthwise distribution of patients. □, Cases examined; ▨, cases of Japanese encephalitis.

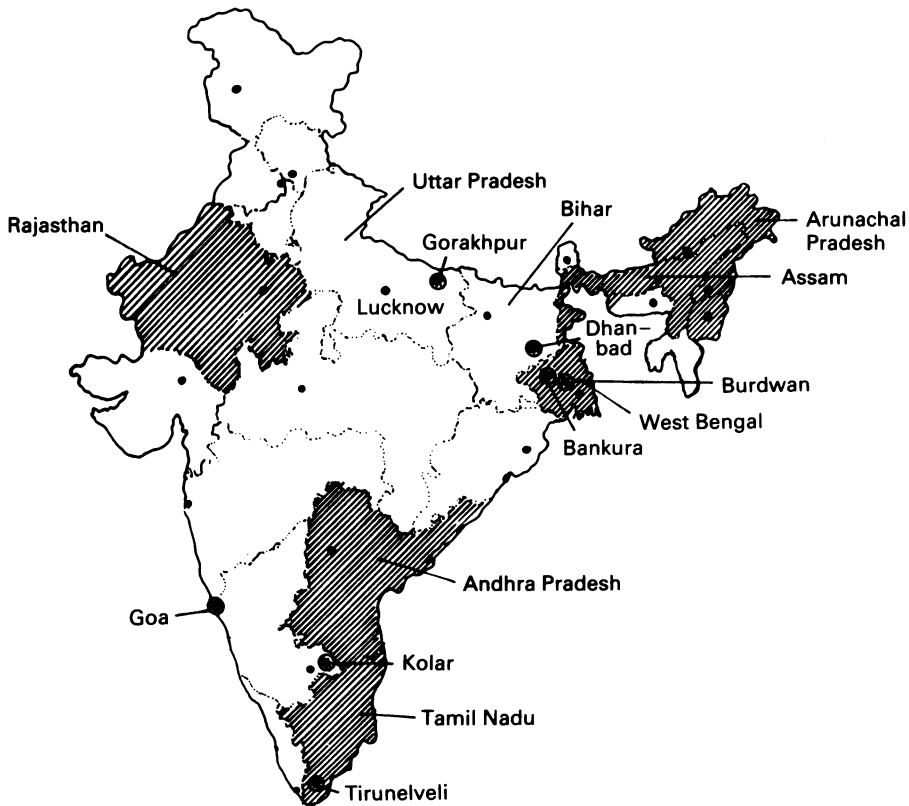
possible to exclude JEV in them as the isolation rate of the virus even in epidemics is not high.<sup>2,3,11</sup> JEV, therefore, is possibly the major cause of acute unexplained encephalopathy in this region. Other viruses such as *Herpes simplex* and enteroviruses can produce a clinically indistinguishable illness. These have been reported from various parts of the country from time to time.<sup>12,13</sup> Again, it may not be possible to firmly exclude certain other conditions such as cerebral malaria and tuberculosis.

The isolation rate of the virus in this study is higher than reported by other workers.<sup>2,3,17</sup> Only patients presenting in the acute phase of the illness were taken for study, when the virus is likely to be more readily isolated from the brain and CSF. Antibodies may not be detectable at this stage. Convalescent sera could be obtained in a relatively small number of cases. This was partly due to the high mortality in the acute stage of the illness.

Infection with JEV is known to occur in Japan, Korea, Taiwan, Vietnam, Thailand and the USSR.<sup>14-16</sup> JEV activity in India was first noted in

the South where the virus was isolated from cases of encephalitis and serological surveys revealed the presence of antibodies to the virus. Specific antibodies to JEV have also been demonstrated in humans in various other parts of the country (Figure 2). In 1973 the first major epidemic was recorded in the Bankura district of West Bengal.<sup>2</sup> Further spread of the virus was evident with the epidemics of 1978 involving Dhanbad in Bihar<sup>11</sup> and Gorakhpur and surrounding districts in Uttar Pradesh.<sup>4</sup> Recurrent outbreaks have since been reported mostly from southern and eastern parts of the country.<sup>17,18</sup> The findings of the present study suggest that JEV is probably endemic in the Lucknow area.

Clinical features of the disease are available from data collected during epidemics. The disease affects all age groups with the highest incidence among children. Males are more frequently affected than females, the male:female ratio being between 1.5:1 and 2:1. The illness is also seen more commonly in people of the lower socio-economic class and rural areas. The course of the disease can be divided into



**Figure 2** Places where outbreaks of Japanese encephalitis have occurred and JEV-specific antibodies have been found in the population. ⊗, Epidemics of JEV; ▨, JEV-specific antibodies in population.

3 stages – a prodromal stage with fever, headache and malaise without signs of central nervous system (CNS) involvement, an encephalitic stage marked by continuing fever and CNS signs like convulsions, coma and focal deficits, and a late stage characterized by gradual recovery over weeks or months or signs of irreversible neuronal damage in the form of sequelae.<sup>19</sup> Mortality rates during epidemics vary between 20 and 50% and another 10 to 20% suffer disabling sequelae.<sup>20</sup>

Studies from peninsular and eastern parts of India indicate that pigs are the main vertebrate hosts of the virus and the major reservoir of the infection.<sup>19</sup> Ardeid birds are also incriminated as vertebrate hosts of JEV. The main arthropod vectors of JEV in India are mosquitos of the *Culex vishnui* complex, especially *Culex tritaeniorhynchus*.<sup>19</sup> Pigs, besides other animals, are widely prevalent in both rural and urban areas of Uttar Pradesh. However, epidemiological and ecological aspects of the illness remain to be studied in this part of the country.

Japanese encephalitis has been seen in travellers to the subcontinent.<sup>21</sup> Travellers are advised to avoid exposure to mosquito bites by means of mosquito repellents and nets. An inactivated vaccine derived from mouse brain is presently available. The vaccine, although not fully protective, is found to reduce the incidence of the disease in the vaccinated population. It is given as 2 doses of 1 ml each (0.5 ml in children below 3 years of age) subcutaneously 7–14 days apart. Booster doses after 1 and 3 years are also given.<sup>19</sup> The vaccine is available at the National Institute of Communicable Diseases in New Delhi.

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