

# **Epidemiology & Health Bulletin**

- 19 A Survey of the Clinical  
Sequelae of Japanese  
Encephalitis  
27 Cases of Notifiable and  
Reportable Diseases,  
Taiwan-Fukien Area
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## **A Survey of the Clinical Sequelae of Japanese Encephalitis**

### **Introduction**

Japanese encephalitis (JE) is a major public health issue. In some areas of Asia — for instance, Thailand, Myanmar, Vietnam, India and Indonesia — the disease is most prevalent and causes serious sequelae in both children and adults<sup>(1)</sup>. The disease was made reportable in Taiwan in 1955 and, to date, some 10 confirmed cases have been reported each year<sup>(6)</sup>. The age of JE patients here seems to have increased in recent years. To better understand the new distribution of cases and their sequelae, a survey was conducted.

JE virus is a kind of RNA virus of the flaviviridae group<sup>(1)</sup>. Though the process is difficult, the virus can still be cultured by using either the kidney cell strain of monkey or the chicken embryo cell. The host and reservoir are either pigs or birds, with the mosquitoes, most commonly *Culex tritaeniorhynchus*, the main vector of transmission. The natural cycle of the virus is this: in late spring and early summer, the virus breeds in either birds or pigs, moves on to mosquitoes whose bite transfers it to other birds and pigs to increase the magnitude of infection. The number of infected mosquitoes reaches peak in mid-summer, and the infection of man then begins. The incubation period is from one to two weeks. In acute onset, patients will have headache for one to three days with occasional nausea or significant loss of body weight. Some 85 to 90% of the JE victims will have high fever and even serious onset of stupor, lethargy or epilepsy. In many children, meningeal symptoms such as stiffness, and even opithotonus, of the neck may develop. Occasionally, some cerebro-nervous and kinetic-nervous symptoms such as facioplegia, clenching of teeth, diplopia, strabismus, nystagmus, dyscatambrosis and dysphagia may occur; some pyramidal and extrapyramidal symptoms such as stiffness or slow movement of the limbs, atrophy and choreoathetosis may also develop<sup>(1,8)</sup>.

Around 25% of all JE patients will develop sequelae. Major categories of sequelae are mental and kinetic<sup>(8)</sup>. Mental sequelae in particular bring misfortune to both patients and their families, and the cost to society for their care is predictably significant.

## Background

JE is a communicable disease which is important to prevent and to control because it has serious sequelae and there is, as yet, no effective cure. Yet this disease can be prevented through immunization<sup>(2)</sup>. Mass immunization of children began in 1986 in Taiwan, and disease incidence has sharply declined since then. Statistics of recent years, however, show that the age of those persons infected has increased. Whether sequelae in these cases are similar to those previously seen is a new concern.

## Materials and Methods

Sequelae of cases confirmed from the years 1991 through November 1994 were surveyed. "Confirmed cases" were those reported by medical care institutions and later proved by serological testing. A case was confirmed when, by use of the hemagglutination inhibition (HI) procedure, the serum antibody titer in the convalescent period was four or more times higher than that during the acute period; when titer in the convalescent period was greater than, or equal to, 1:160; or when one-time serum HI antibody titer was greater than, or equal to, 1:320. Reported cases were interviewed at home with a structured questionnaire. Questions asked could also be answered by family members and included data on personal background, date of onset, personality and mental reactions before and after onset. Neurological examinations including 12 pairs of cerebro-nerves, motor functions, sensory functions, reflection, autonomic nerve functions and judgment orientation memory affecting calculation (JOMAC) testing were done to explore the sequelae of confirmed cases. A total of 59 cases (29 in 1991, 9 in 1992, 8 in 1993 and 13 in 1994) were surveyed (see Figure 1). History of immunization was confirmed by the records kept in the health stations of Taiwan province but, in Taipei City, immunization records are kept for 10 years; thus the immunization history of some cases was necessarily listed as "Unknown".

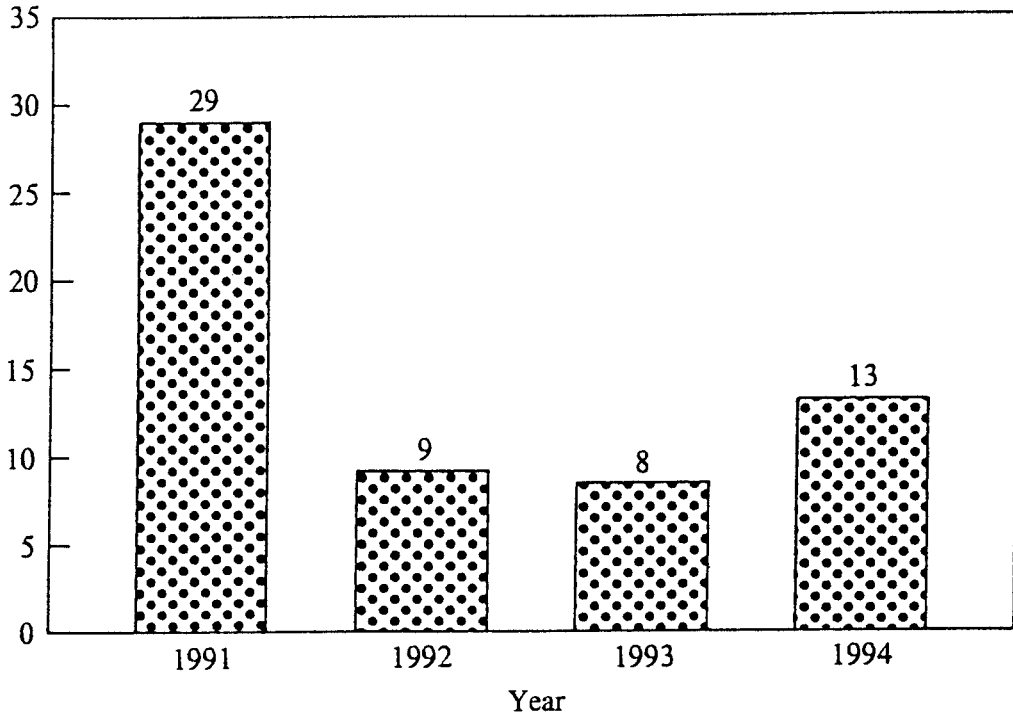
## Findings

Ages of confirmed cases ranged from 6 to 64 years, averaging 24.33 year; male to female ratio was 2:1. Of those surveyed, 8 were aged 9 years and under (13.6%); 13, in the 10-19 age group (22.0%); 19, in the 20-29 age group (32.3%); 12, in the 30-39 age group (20.3%); 4 in the 40-49 age group (6.8%); 2 in the 50-59 age group (3.4%) and 1, in the 60-69 age group (1.7%) (see Figure 2). Most cases were in the 10-39 age groups.

Of those surveyed, 34 (57.6%) had never had any immunization, 3 (5.1%) had had 1 dose, 4 (6.8%) had received 2 doses, 3 (5.1%) had had 3 doses, 5 (8.5%) had had 4 doses, and 10 (17.0%) lacked immunization information.

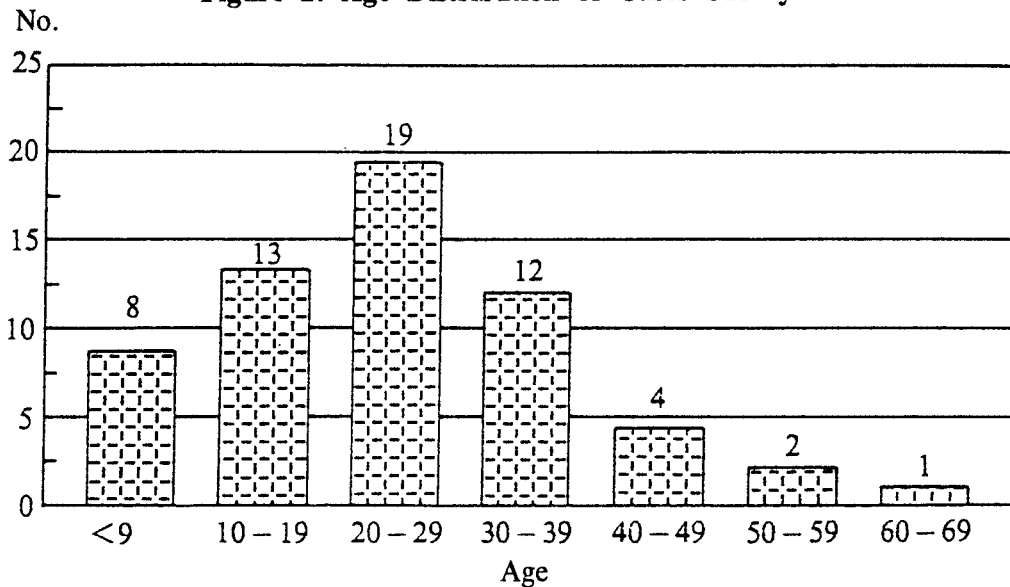
Sequelae surveyed included neurological function impediments and mental

No. **Figure 1. Number of Cases Surveyed by Year, 1991-1994, N=59**



Date of Survey: November-December 1994

**Figure 2. Age Distribution of Cases Surveyed**



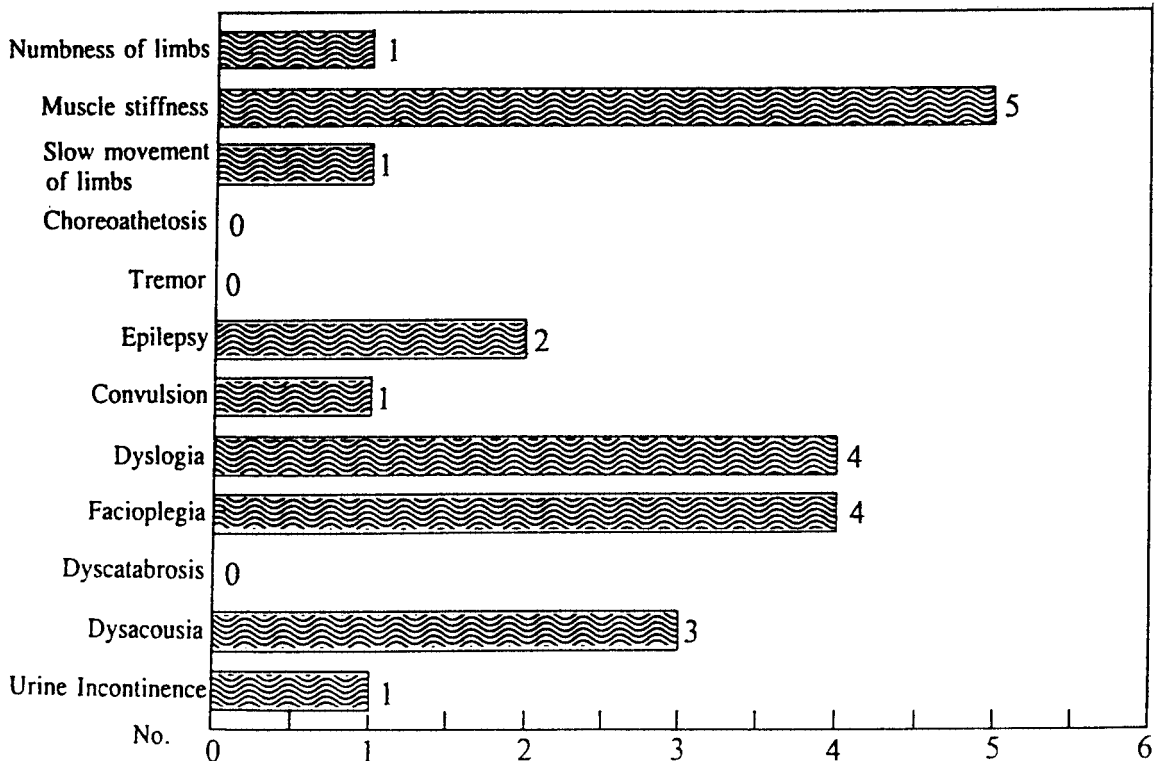
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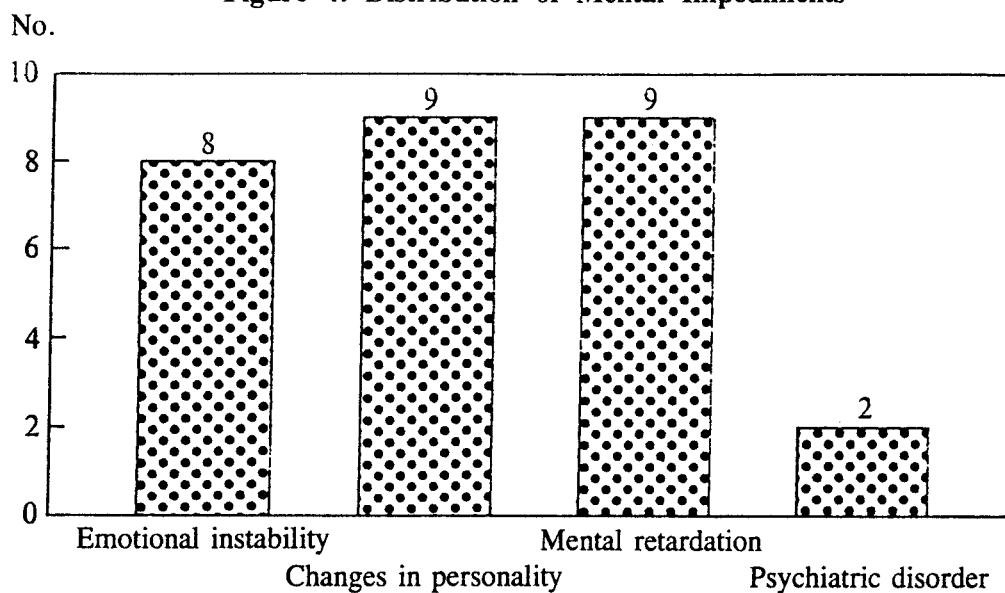
impediments. A patient would often have many sequelae. The impediments of neurological functions included one (1.7%) with numbness of limbs; five (8.5%) with muscle stiffness, one (1.7%) with slow movement of limbs. None had either choreoathetosis or tremor but two (3.4%) had epilepsy, one (1.7%) had convulsions, four (6.8%) had dyslogia, four (6.8%) had facioplegia; none had dysphagia, three (5.1%) had dysacousia and one (1.7%) had urine incontinence. As to mental impediments, eight (13.6%) were emotionally unstable, nine (15.3%) showed changes in personality, nine (15.3%) had indications of mental retardation, and two (3.4%) became psychotic (see Figures 3 and 4).

Sequelae, including both kinetic and mental as observed in cases by year, showed that of the cases in 1991, three still had either kinetic or mental sequelae (10.3% of all cases they year), three in 1992 still had one or the other of the sequelae (22.2%), one in 1993 still had one or the other (12.5%), and five in 1994 still had either sequele (38.4%).

Seven male cases (17.9% of total male cases) and four female cases (20.0% of total female cases) had sequelae.

**Figure 3. Distribution of Impediments of Neurological Functions**



**Figure 4. Distribution of Mental Impediments**

By age, 1 case in 0-9 age group (12.5% of all cases in this age group), 3 in 10-19 age group (23.0%), 4 in 20-29 age group (21.0%), 2 in 30-39 age group (16.7%), 1 in 40-49 age group (25.0%), none in 50-59 age group, and none in 60-69 age group had sequelae.

By immunization history, of those with sequelae, seven had never been immunized (63.7%), two of those had had one dose (18.1%), one had had one dose (9%), one had had three doses (9%), and none of those receiving four doses had sequelae (see Table 1).

**Table 1. Cases by Immunization History**

Immunization Status	No.	%
Never immunization	34	57.6
One dose	3	5.1
Two doses	4	6.8
Three doses	3	5.1
Four doses	5	8.5
Unknown	10	16.9
<b>Total</b>	<b>59</b>	<b>100.0</b>

Never immunized: persons without immunization records

Unknown: immunization records not found

Note: more than half of the cases had not been immunized.

## Discussion

Both the epidemiological patterns and distribution of Japanese encephalitis have changed in recent years. In Taiwan and in neighboring Japan and Korea, the incidence has declined sharply. In Taiwan for instance, changes in farming practice and the reduction in arable land, use of pesticides, promotion of large-scale pig farms and mass immunization programs may have been the reasons<sup>(4)</sup>. Though incidence has declined, Japanese encephalitis definitely occurs each year during summertime and has become an endemic disease in Taiwan. Each year, some 10 confirmed cases are reported<sup>(5)</sup>. In the present survey, the peak age for confirmed cases was in the 20-29 age group, followed by the 10-19 and 30-39 age groups. The ages of confirmed cases seem to have increased, a change perhaps resulting from urbanization and the decline in the number of vectors. With fewer chances of being bitten by mosquitoes, chances of developing active immunity have also declined. Thus some older persons may not develop immunity against JE.

Most of the cases, (34, or 57.6%) were among those who had never been immunized. Immunization history was checked against the records of health stations. Since Taipei City kept immunization records for only 10 years, the status of some cases was necessarily listed as "Unknown".

There were more mental sequelae than sequelae of neurological functions. Kinetic function impediments caused by neurological impairment can be restored through rehabilitation and, when patients are generally more cooperative, their chances for improvement are greater. The percentage of cases with neurological sequelae, according to reports from all cases in 1991 (10.3%), was lower when compared with 1994 (38.4%,  $p < 0.05$ ). This fact seems to indicate that retention of sequelae is related to the four-year period since disease onset. However, if the four-year period as a whole is compared, the relationship between retention of sequelae and duration since onset is not clear. That is, the inference that sequelae will improve with time requires more and longer - term observation. Mental sequelae including emotional instability, changes in personality, mental retardation and psychiatric disorders (one was manic-depressive and the other, schizophrenic) lasted longer.

Neither sex nor age was found to be related to sequelae ( $p > 0.05$ ). Age does not necessarily facilitate the retention of sequelae. Though in the present survey, immunization and the number of doses were not found to be significantly related to sequelae ( $p > 0.05$ ), none of those who had had four doses had developed any sequelae.

## Limitations of the Survey and Survey Methods

Of the 68 confirmed cases, 1 died and 8 were either not met or refused interview. Thus only 59 cases, or 86.7%, were in fact interviewed.

Of the instances of mental sequelae, two patients who were already mentally

retarded were not included in the cases with mental sequelae. Information concerning mental conditions prior to onset was not available; to decide whether mental retardation had taken place, either school records were compared or statements of family members were used, calling into question accuracy of judgment. Accuracy would be higher if more precise assessment could be made of cases suspected of having mental sequelae.

### Recommendations

The present survey noted a significant increase in the age of Japanese encephalitis infection victims. More studies therefore are needed to understand the neutralization antibody titer in each age group and the antibody retention rates of natural, inapparent infections; and to decide whether the high risk groups are now older people and, if so, whether immunization should be provided for these groups.

Another finding of the survey was that most neurological function sequelae noted in the acute period had disappeared by the time of interview. This seems to indicate that neurological function sequelae are partially restored to normalcy with time or rehabilitation. More follow-up study is, therefore, recommended to confirm that finding in order to make more appropriate rehabilitation recommendations. More studies are also recommended to understand whether neurological function sequelae in fact improve with time.

It would be more desirable if HI procedures and neutralization antibody testing could be applied jointly for reliable confirmation of cases<sup>(7)</sup>.

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