Neurological Sequelae of Hospitalized Japanese Encephalitis Cases in Gansu Province, China

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Abstract. We conducted a follow-up survey for 55 Japanese encephalitis (JE) cases 1–2 years after hospital discharge in Gansu province, China. Community-, education-, and gender-matched healthy individuals without history of neurologic disease were selected as the comparison group. All subjects received neurological examination, intelligence quotient (IQ) measurement, adaptive behavior measurement, and Wechsler memory scale (WMS) assessment. We found 43.6% JE cases had at least one nervous system sequelae compared with 3.6% healthy individuals. Among JE cases, 22.4% had subnormal IQ, 18.4% subnormal verbal IQ (VIQ), 20.4% subnormal performance IQ (PIQ), and 78.4% had subnormal memory quotient (MQ). Among healthy individuals, 2.0% had subnormal IQ, VIQ, or PIQ and 8.1% had subnormal MQ. Among adult JE cases, 47.8% and 39.1% had adaptive behavior impairments and intellectual disability, respectively, compared with 18.8% and 9.7% among young cases, respectively. The results showed both adult and young surviving JE cases had significant neurological sequelae and mental disability 1–2 years after discharged.

INTRODUCTION

Japanese encephalitis (JE) virus, a mosquito-borne flavivirus, is the most common cause of encephalitis in Asia.¹ Among JE patients, 20–30% die and 30–50% of survivors have significant neurological sequelae.² Approximately 67,900 JE cases occur annually, of which only about 10% are reported to the World Health Organization. Most of these cases occur in China,³ as JE is highly endemic in China. Devastating epidemics occurred in the 1960s and 1970s, with the highest reported incidence reaching 20.9 cases/100,000 population in 1970. The incidence rate has decreased substantially since the 1980s, when JE vaccines were introduced for children ≤ 10 years of age.⁴ From 1981 through 2007, parents had to pay for JE vaccine since it was not included in the Expanded Program on Immunization (EPI) in Gansu province, China. Consequently, JE vaccination coverage was very low for children under 15 years of age among those seen at local Center for Disease Control (CDC) immunization clinics.⁵

With the wide use of JE vaccines in China, most cases among young children have been prevented by immunization. However, the proportion of the cases occurring among the elderly patients has increased in many areas, especially in Shanghai and in some developed cities in Shanxi and Shandong provinces.^{6–8} A similar pattern was found in Korea and in Japan where the previous bimodal age distribution of cases, with peaks in young children and in the elderly, has shifted toward a predominance of cases in adults.^{9,10} This shift may not mean an absolute increase in the number of cases in older populations, but it has resulted in more attention to the epidemiology and public health disease burden in among elderly JE cases.

In September 2007, we conducted an investigation of neurologic and cognitive sequelae for JE cases from three prefectures in Gansu province. The main objectives of this study were to assess the disability and sequelae of JE, especially, the adult JE cases, to estimate the relative importance and to determine whether JE prevention among adults should be

regarded as a public health priority. We present the results of this controlled neurological sequelae survey of JE cases.

MATERIALS AND METHODS

Inclusion and follow-up of the JE cases. In November 2007, we conducted a retrospective review of JE cases reported in 2005 or 2006 in the China National Notifiable Disease Reporting System (NNDRS) by Tianshui, Pingliang and Longnan prefectures, Gansu province. We selected laboratory-confirmed JE cases as subjects. Laboratory confirmation of JE was performed by prefecture CDC laboratories with JE virus IgM enzyme-linked immunosorbent assay (ELISA) testing conducted on all cerebrospinal fluid (CSF) or serum samples, using the recommended JE Virus IgM-Capture ELISA kit (Beixi Kit; Shanghai B&C Biological Technology Co., Ltd., Shanghai, China).

Inclusion of the healthy group. We selected the healthy individuals from the same community as JE cases under the help of the community or village doctors according to the living address, but without history of previous neurological disease. The healthy individuals were matched on gender and educational level with the JE cases. The ages of the healthy individuals were similar to the ages of the JE cases. Age differences were limited < 1 year for toddlers (≤ 6 years old), < 2 years for children (7–15 years old), and < 3 years for adult (≥ 16 years) between case group and healthy group.

Assessments and testing to the JE cases and healthy individuals. For each JE case and healthy individual, a comprehensive neurological examination and intellectual assessment was conducted. Neurological examinations were conducted by neurologists blinded to prior disease status, which included muscle strength, muscle tone, muscle feeling, tendon reflexes and pathological reflex, aphasia, cranial nerve system symptoms (dysphagia, salivation, lisping, vision loss, hearing loss), mental state, and with/without epilepsy. A case or healthy individual with any of these disorders was considered to have neurological conditions.

Intelligence testing was performed using the China Wechsler Young Children Scale of Intelligence (C-WYCSI, for 4–6 years old young children), the China Wechsler Intelligence Scale for Children (C-WISC, for 6–15 years old children), or the

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TABLE 1
Demographic characteristics of JE cases in Longnan, Pingliang, and Tianshui prefectures in Gansu province, 2005–2006

	Pingliang			Tianshui			Longnan			Total		
	Tested JE cases	No. of JE (+) (%)	Followed up of JE (+) (%)	Tested JE cases	No. of JE (+) (%)	Followed up of JE (+) (%)	Tested JE cases	No. of JE (+) (%)	Followed up of JE (+) (%)	Tested JE cases	No. of JE (+) (%)	Followed up of JE (+) (%)
Ages (years)*												
0–5	6	3 (50.0)	3 (100.0)	4	4 (100.0)	3 (75.0)	17	10 (58.8)	8 (80.0)	27	17 (63.0)	14 (82.5)
6–14	5	3 (60.0)	2 (66.7)	11	7 (63.6)	5 (71.4)	21	17 (81.0)	11 (64.7)	37	27 (73.0)	18 (66.7)
15–77	37	29 (78.4)	10 (34.5)	14	12 (85.7)	3 (25.0)	26	18 (69.3)	10 (55.6)	77	59 (76.6)	23 (39.0)
Total	48	35 (72.9)	15 (42.9)	29	23 (79.3)	11 (47.8)	64	45 (70.3)	29 (64.4)	141	103 (73.0)	55 (53.3)
Sex												
Male	22	14 (63.6)	6 (42.9)	15	11 (73.3)	7 (63.6)	35	25 (55.6)	16 (64.0)	72	50 (69.4)	29 (58.0)
Female	26	21 (80.8)	9 (42.9)	14	12 (80.0)	4 (33.3)	29	20 (44.4)	13 (65.0)	69	53 (76.8)	26 (49.1)
Living place												
Rural	40	29 (72.5)	12 (41.4)	24	18 (75.0)	9 (50.0)	63	44 (69.8)	29 (65.9)	127	91 (71.7)	50 (55.0)
Urban	8	6 (75.0)	3 (50.0)	5	5 (100.0)	2 (40.0)	1	1 (100.0)	0	14	12 (85.7)	5 (41.7)

JE (+) = Japanese encephalitis positive.

Wechsler Adult Intelligence Scale Revised in China (WAIS-RC, for ≥ 16 years old people) amended by Gong Yaoxian from Hunan Medical University. The intelligence testing included verbal and performance scales testing. Intelligence quotient (IQ) was generated by looking up table, based on the results of the verbal IQ (VIQ) and performance IQ (PIQ).

The Children's Adaptive Behavior Assessment Scale (CABAS) and the Adult Intellectual Disability Assessment Scale (AIDAS), amended by Yao Shuqiao from Hunan Medical University, were used to test the intellectual disability scales for those who had suspected intellectual disability or were not able to complete the intelligence test because of severe mental retardation. This test was only conducted for JE cases.

The Wechsler Memory Scale (WMS, types A and B) amended by Gong Yaoxian from Hunan Medical University was used to assess memory ability (including short-term, mid-term, and long-term memory ability) for ≥ 7 years old subjects. A comprehensive memory quotient (MQ) was derived from these test results.

Ethical considerations. The ethical review committee at the Gansu Provincial CDC approved the survey, and written informed consent was obtained from the JE cases and healthy individuals or from their proxies before the investigation.

Data collection and analysis. Demographic, examination, and testing data from JE cases and healthy individuals were entered in an EPIDATA database. For comparison of the results of the neurological examinations at discharge and follow-up, and of the results of psychological assessment

between JE cases and healthy individuals by age group, the Chi square (χ^2) or Fisher exact test for the rates or percentage in different groups and student's *t* test or Kruskal–Wallis test for means were used.

Quality control. Trained experts and clinical doctors conducted all surveys, examinations and assessments. We also used questionnaires of type A or B of WMS to avoid bias when the JE cases and healthy individuals were tested.

RESULTS

Follow-up and demographic features of JE cases. The reported 206 JE cases included 11 suspected cases, 92 clinically diagnosed cases, and 103 laboratory-confirmed cases in years 2005 and 2006 from the 3 prefectures. Among the 103 laboratory-confirmed JE cases (59 adults and 44 children), we followed up 55 cases (3 cases occurred in year 2005 and 52 cases occurred in year 2006), as 22 cases refused, 20 died of JE, and 6 cases without contact information were all lost to follow-up. Among the 20 dead JE cases, there were 18 dead cases ≥ 15 years of age and 2 dead cases < 15 years of age. The fatality rate for JE cases ≥ 15 years (30.5%, 18/59) were significantly higher than that for JE cases < 15 years (4.5%, 2/44) because of the JE illness or other unrelated causes before the study follow-up. Of the remaining 41 eligible adult cases, 23 (56%) were enrolled. Of the remaining 42 eligible pediatric cases, 32 (76%) were enrolled. The proportion of eligible children enrolled was clearly higher than that of eligible adults, but was not statistically significant.

TABLE 2
Results of the neurological examinations of the survived JE cases at discharged and at followed up by age group

Examination	Discharge				Followed up				χ^2 test	P value
	2–5 years N = 14 (%)	6–14 years N = 18 (%)	≥ 15 years N = 23 (%)	Total N = 55 (%)	2–5 years N = 14 (%)	6–14 years N = 18 (%)	≥ 15 years N = 23 (%)	Total N = 55 (%)		
Neurological										
Disturbance of consciousness	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	N/A	
Meningeal irritation	3 (21.4)	0 (0)	2 (8.7)	5 (9.1)	0 (0)	0 (0)	0 (0)	0 (0)	*	0.028
Cranial nerves symptoms	2 (14.3)	5 (27.8)	11 (47.8)	18 (32.7)	0 (0)	1 (5.6)	3 (13.0)	4 (7.3)	11.0	0.001
Motor neuron symptoms	7 (50.0)	7 (38.9)	13 (56.5)	27 (49.1)	4 (28.6)	4 (28.6)	9 (39.1)	17 (30.9)	3.07	0.08
Aphasia	1 (7.1)	1 (5.6)	2 (8.7)	4 (7.3)	1 (7.1)	0 (0)	3 (13.0)	4 (7.3)	0	1.000
Epilepsy	0 (0)	0 (0)	0 (0)	0 (0)	1 (7.1)	1 (5.6)	0 (0)	2 (3.6)	†	0.495
Mental disorders	1 (7.1)	1 (5.6)	3 (13.0)	5 (9.1)	0 (0)	2 (11.1)	6 (26.1)	8 (14.5)	0.8	0.378
With any of above	8 (57.1)	10 (55.6)	17 (73.9)	35 (63.6)	7 (50.0)	6 (33.3)	11 (47.8)	24 (43.6)	4.4	0.036

χ^2 tests were conducted only for the total cases when discharged and followed up.

*Fisher test with one-tailed P value.

†Fisher test with two-tailed P value.

The seropositive rate for the JE cases with laboratory testing in the three prefectures was 73.0% (55/141, with a range of 70.3–79.3%). The percentage of the JE cases followed up averaged 53.3% (55/103), and follow-up was more complete for children aged 6–14 years (66.7%, 18/27) and for children aged < 5 years (82.5%, 14/17) than for adults (39.0%, 23/59).

Among the 55 JE cases followed up, 41.8% (23/55) were ≥ 15 years old, 52.7% (29/55) were male, and 90.9% (50/55) were living in rural areas (Table 1).

Neurological sequelae findings for the JE cases and healthy individuals. Among the 55 JE cases, no cases had disturbance of consciousness when discharged from the hospitals or at follow-up. Five (9.1%) cases had meningeal irritation when discharged, but none had this sign at follow-up. The main neurological sequelae were motor neuron symptoms, which we found in 27 (49.1%) cases at discharge and 17 (30.9%) cases at follow-up. The main clinical features for the cases with motor neuron symptoms were paralysis, hemiplegia, and limb movement disorder, such as reduced muscle strength, tendon reflexes, involuntary movements, and increased muscle tone when followed up. Cranial nerve symptoms, including dysphagia, salivation, lisping, vision loss, hearing loss, were improved significantly, reduced from 32.7% (18/55) after discharge from the hospitals to 7.3% (4/55) when followed up. We also found 2 (3.6%) cases with epilepsy and 8 (14.5%) cases with mental disorders when followed up. Overall, 1–2 years after discharge from the hospitals, 43.6% (24/55) of surviving JE cases still had at least one nervous system sequelae, compared with 63.6% (35/55) at hospital discharge (Table 2).

In the healthy group, we only found that 2 individuals (3.6%) had the neurological symptom, both of them had reduced tendon reflex. The percentage of neurologic symptoms was significantly lower than that seen in the JE group with at least one nervous system when followed up (43.6%, $\chi^2 = 24.16$, $P = 0.00$).

We compared rates of any neurological sequelae and mental disorders by the different age groupings when followed up, and found that adult (≥ 15 years) JE cases had overall rate of any of the neuropsychiatric sequelae (47.8%, 11/23) at similar rates as the 2–5 (50.0%, 7/14) and 6–14 (33.3%, 6/18) years group of the JE cases ($\chi^2 = 1.17$, $P = 0.56$).

Intelligence assessment for JE cases and healthy individuals.

In total, 49 pairs of cases and healthy individuals underwent intelligence testing. Six JE cases did not receive intelligence testing, 1 case was < 4 years old and was therefore ineligible, and other 5 cases, including 1 case of 8 years of age and 4 cases of ≥ 15 years of age had severe mental impairment and were unable to participate in the testing.

The average IQ, VIQ, and PIQ scores were significantly lower in JE cases than in healthy individuals, except for IQ and VIQ in 6–14 years group (Table 3).

Among the JE cases, 11 (22.4%) had IQ scores < 70, 9 (18.4%) had VIQ scores < 70, and 10 (20.4%) had PIQ scores < 70. In healthy individuals, we found only 1 (2.0%) with IQ, VIQ, or PIQ scores < 70. The proportion of lower IQ, VIQ, and PIQ in JE group were significantly higher than in healthy individuals, except VIQ in the 2–5 years group (no significant difference between the JE cases and healthy groups) (Table 4). When five JE cases with severe mental impairment (assessment results: all below mild mental disability) were included, the overall proportion of mental retardation (IQ scores < 70) in JE cases group was 29.6% (16/54).

TABLE 3
Comparison results of psychological assessment between JE cases and healthy individuals by age group

Examination	2–5 years (N = 13)			6–14 years (N = 17)			≥ 15 years (N = 19)			Total (N = 49)		
	JE group ($\pm s$)	Healthy group ($\pm s$)	<i>t</i> test	JE group ($\pm s$)	Healthy group ($\pm s$)	<i>t</i> test	JE group ($\pm s$)	Healthy group ($\pm s$)	<i>t</i> test	JE group ($\pm s$)	Healthy group ($\pm s$)	<i>t</i> test
IQ	80.9 $\pm$ 21.0	104.5 $\pm$ 20.8	-4.8	100.5 $\pm$ 16.2	108.0 $\pm$ 17.9	-1.7	82.9 $\pm$ 17.7	98.5 $\pm$ 15.4	-3.1	88.5 $\pm$ 19.9	103.4 $\pm$ 17.9	-5.2
VIQ	87.8 $\pm$ 21.5	104.8 $\pm$ 23.7	-3.4	107.6 $\pm$ 20.6	111.5 $\pm$ 17.8	-0.7	85.3 $\pm$ 23.9	98.1 $\pm$ 15.0	-2.1	93.7 $\pm$ 24.0	104.5 $\pm$ 19.1	-3.2
PIQ	76.4 $\pm$ 18.9	102.0 $\pm$ 15.7	-5.6	92.8 $\pm$ 14.1	102.8 $\pm$ 17.8	-2.4	82.9 $\pm$ 17.7	98.3 $\pm$ 18.0	-2.9	84.6 $\pm$ 17.8	100.9 $\pm$ 17.1	-5.7
P value												
	0.00	0.00	0.01	0.01	0.11	0.50	0.03	0.05	0.01	0.01	0.00	0.00

JE = Japanese encephalitis positive; IQ = intelligence quotient; PIQ = performance intelligence quotient; VIQ = verbal intelligence quotient.

TABLE 4
Comparison results of psychological assessment between JE cases and healthy individuals by age group

Examination	2-5 years (N = 13)				6-14 years (N = 17)				≥ 15 years (N = 19)				Total (N = 49)			
	JE group	Healthy group	χ^2 test	P value	JE group	Healthy group	χ^2 test	P value	JE group	Healthy group	χ^2 test	P value	JE group	Healthy group	χ^2 test	P value
IQ																
≥ 70 (%)	9 (69.2)	13 (100)	*	0.048	16 (94.1)	17 (100)	*	0.500	13 (68.4)	18 (94.7)	*	0.045	38 (77.6)	48 (98.0)	9.4	0.002
< 70 (%)	4 (30.8)	0			1 (5.9)	0			6 (31.6)	1 (5.3)			11 (22.4)	1 (2.0)		
VIQ																
≥ 70 (%)	10 (76.9)	13 (100)	*	0.110	16 (94.1)	17 (100)	*	0.500	14 (73.7)	18 (94.7)	*	0.090	40 (81.6)	48 (98.0)	7.1	0.008
< 70 (%)	3 (23.1)	0			1 (5.9)	0			5 (26.3)	1 (5.3)			9 (18.4)	1 (2.0)		
PIQ																
≥ 70 (%)	9 (69.2)	13 (100)	*	0.048	16 (94.1)	17 (100)	*	0.500	14 (73.7)	18 (94.7)	*	0.090	39 (79.6)	48 (98.0)	8.2	0.004
< 70 (%)	4 (30.8)	0			1 (5.9)	0			5 (26.3)	1 (5.3)			10 (20.4)	1 (2.0)		
MQ																
≥ 70 (%)	0	2 (100)	*	0.167	3 (18.8)	16 (100)	21.2	0.000	5 (26.3)	16 (84.2)	12.5	0.000	8 (21.6)	34 (91.9)	36.7	0.000
< 70 (%)	2 (100)	0			13 (81.2)	0			14 (73.7)	3 (15.8)			29 (78.4)	3 (8.1)		

JE = Japanese encephalitis positive; IQ = intelligence quotient; PIQ = performance intelligence quotient; VIQ = verbal intelligence quotient.

*Fisher test with one-tailed P value.

Comparing the prevalence of lower IQ, VIQ, and PIQ scores (< 70) in adult JE cases (aged ≥ 15 years) with that in young JE cases (< 15 years), there were no significance between the two groups (6/19 versus 5/30, $\chi^2 = 1.46$, $P = 0.23$; 5/19 versus 4/30, $\chi^2 = 1.28$, $P = 0.26$; 5/19 versus 5/30, $\chi^2 = 0.65$, $P = 0.42$, respectively).

Memory assessment for JE cases and healthy individuals.

Among the 55 JE case healthy individual pairs, we conducted memory assessment for 37 JE cases and healthy individuals who were aged ≥ 7 years when followed up; 12 JE cases < 7 years were ineligible for testing; and 6 JE cases could not complete testing because of the severe mental impairment. Overall, 78.4% (29/37) of JE cases had MQ scores < 70, compared with only 8.1% (3/37) in the healthy individuals ($\chi^2 = 36.72$, $P = 0.00$) (Table 4).

Comparing the prevalence of lower MQ scores (< 70) in adult JE cases (aged ≥ 15 years) with that in young JE cases (< 15 years), there was no significance between the two groups (14/19 versus 15/18, Fisher exact test, $P = 0.69$).

Adaptive ability evaluation for JE cases. We conducted an adaptive behavior level test for 12 children (< 15 years of age) who were possibly judged as mentally retarded in the intelligence testing. Four JE cases were normal and two were on the threshold of mental disability, three showed mild mental disability, two showed moderate mental disability, and one case showed severe mental disability. The prevalence of adaptive behavior impairment for case children was 18.8% (6/32).

We also conducted an adaptive behavior level test for 11 adult (≥ 15 years of age) JE cases. Six were classified as having mild mental disability, two moderate mental disability, two severe mental disability, and one case was classified with highly severe mental disability. The prevalence of adaptive behavior impairment for adult cases was 47.8% (11/23).

Intellectual disability assessment for JE cases. We conducted an intellectual disability assessment for 54 JE cases. A total of 12 (12/54, 22.2%) JE cases were judged as mentally disabled. Among the 12 JE cases, the prevalence of intellectual disability in adult cases (9/23, 39.1%) was higher than that in young children (3/31, 9.7%) cases ($\chi^2 = 6.60$, $P = 0.01$).

DISCUSSION

This is the first neurological sequelae survey of JE in Gansu province. JE mainly affects children, and most of the JE

studies in China have focused on children. In this study, we found that JE infection was associated with a high frequency of long-term disability with neurological and mental impairment, subnormal intelligence, including lower IQ, VIQ, PIQ, and MQ for both young children and adult cases. These findings provide more information for the measurement of JE disease burden, especially for JE in adults.

Among the surviving cases 1–2 years after discharged from the hospitals, 43.6% had at least one nervous system sequelae. Since at hospital discharge, 63.6% of cases had neurologic sequelae, our study shows evidence that some neurological sequelae resolve. The survivors' disability rate was similar to survivor disability rates seen in India and Vietnam (45.5–58.0%).^{11,12} We found that motor neuron symptoms were paralysis, hemiplegia, and limb movement disorder such as reduced muscle strength, tendon reflexes, involuntary movements, increased muscle tone, and sensory dysfunction were the most common neurological sequelae for JE cases. Rates of neurological sequelae were very high at discharge and showed no apparent improvement with 1–2 years after discharge. The disability rates of cranial nerve symptoms, such as dysarthria and drooling were higher when discharged from the hospital, when compared with followed up. However, other cranial nerve symptoms of intermittent visual problems and decreased vision occurred in some cases at follow-up.

Previous studies found that young children (< 10 years old) are more likely to have residual neurological impairments than adults, and that severity may vary by age.^{9,11–16} In our study, however, we found that rates with any neurological sequelae and mental disorders among adult (≥ 15 years old) JE cases was similar to that in the young (2–5 years and 6–14 years groups) JE cases. Differences of our results from other studies in disability rates may be due to whether the formal examination has been used or the number of surviving JE cases has been surveyed.

For cognitive functions, the average scores of IQ, VIQ, and PIQ in JE cases were generally lower than in healthy individuals. The prevalence of lower IQ (< 70) was between the lower (14.1%) and higher (32.0%) values obtained in the previous studies.^{17,18} The high prevalence of lower VIQ and PIQ in the 2–5 years and ≥ 15 years groups, suggest that neurological damage of JE involves the entire brain (left brain for verbal functions and the right brain for operational functions).

The prevalence of adaptive behavioral defects in children was lower than that in adults, but was similar to the rate of abnormal activities of daily living (ADL) of JE cases (15.4%).¹⁷ Severe defects in intellectual disability were also seen among adults. These results show that mental disability among adult JE cases was more severe than that among young JE cases.

The prevalence of lower MQ, including long-term, short-term, and instant memory deficits for JE cases were greater than for healthy individuals. All JE cases with IQ < 70 had MQ scores < 51 or failed to complete the memory tests, suggesting the memory impairments may be one of the main features of mental disability.¹⁹

Our study has some limitations. First, we did not enroll all the JE cases. Some JE cases refused to participate, even though we interviewed and examined the JE cases in their county's CDCs for their convenience. The main reasons for refusal included that some cases were living in distant mountain areas and were unable to come to the CDC, were too weak to go outside, or were unwilling to accept medical examination. A second limitation was that we only followed up JE cases 1–2 years after the discharge. There are many factors influencing intelligence, memory, and other psychological constructs. Although we used the more time-consuming Wechsler Intelligence Scale, matched with healthy individuals, and tried to get accurate results of the assessment, neurological sequelae may occur subsequently in cases that were considered normal during this study period. Lower intelligence may be observed if followed up for longer time.

JE is a major public health problem that is controllable by proven, effective vaccines.⁹ It is the leading recognized cause of childhood encephalitis in Asia.¹ In some areas where childhood cases have been greatly reduced by immunization with vaccines, the age distribution of cases has shifted toward adults, and particularly to elderly adults.^{8,10,20} However, the relative importance of JE in adults has yet to be addressed as a public health priority because of lack of data on disease burden, incidence, and outcome.⁹ Our study reveals a high frequency of long-term neurological sequelae and a great disease burden caused by JE for both children and adults, although the JE cases may also show limited improvement over time. We suggest that population and laboratory-based surveillance should be conducted to measure JE incidence in both children and adults, and to continue follow-up observation and analysis to improve our understanding of the cost-effectiveness with newer JE vaccines.

Received March 11, 2014. Accepted for publication March 4, 2015.

Published online April 27, 2015.

Acknowledgments: We thank Jun Li (previously at Mental Health Science Center, Peking University) and Junfeng Yang (previously at National Immunization Programme, China CDC). We also thank Rodewald Lance at World Health Organization China Office, Stephen C. Hadler and Marc Fisher at U.S. CDC. We are grateful for the contributions of the staff at China CDC and Gansu provincial CDCs; the Longnan, Pingliang, and Tianshui prefecture CDCs; the county CDCs, as well as the clinical doctors and patients whose support and participation made this investigation successful.

Financial support: This work was funded by China CDC.

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