

## A Follow-up Study of Japanese B. Encephalitis in Northern Thailand

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**OBJECTIVE:** The study is designed so that answers to the following questions were approached :

a. How many cases of Japanese B. Encephalitis presented as acute psychoses to the major psychiatric hospital in the Chiang Mai area? How are these cases evaluated and to what extent was there misdiagnosis to these cases?

b. What are the mental status changes in the encephalitis convalescent cases? How do these mental status changes affect the functioning of the convalescent patient, and what is the progression of recovery, extent of recovery, and duration of abnormalities in the convalescent encephalitis patient?

c. What are the nature of the EEG changes in convalescent encephalitis patients? What is the duration of these changes?

d. What are the nature, duration, and progression of improvements in neurological deficits manifested by convalescent encephalitis patients?

e. What antibody titer changes occur in the convalescent encephalitis patient? Are there any correlations between these changes and the clinical changes in the convalescent encephalitis patient?

f. What is the effect and reaction on home environment on the convalescent encephalitis patient? How does the home environment influence the behavior of the convalescent encephalitis patient?

g. What is the effect and reaction of school (job) environment on the convalescent encephalitis patient? How does the school (job) environment influence the behavior of the convalescent encephalitis patient?

**DESCRIPTION:** In the 1969 encephalitis epidemic in Northern Thailand, several hundred cases of encephalitis were reported of which 20-25% died. Of the surviving convalescent cases, less than 20 were followed for any significant length of time. After reviewing these cases several tentative impressions were offered by Chiang Mai physicians:

1. return to school (job) at an early stage of convalescence seemed to be associated with more rapid improvement in psychological as well as neurological symptoms;

2. when the symptoms of encephalopathy abated in adult patients, agitated depressive symptoms often followed;

3. among children, the disturbing patterns of motor deficiency (spasticity and rigidity), dyslexia, dysarthria, memory defects, blocking of speech, temper tantrums, retardation, emotional lability and nightmares were common.

4. the E.E.G. changes were typical of any encephalitis, and these abnormal patterns persisted much longer than clinical signs and symptoms.

Ecological studies of Japanese B. encephalitis as reported in other parts of this report were in the planning phases at the time this project was considered. The study of the clinical aspects of the acute encephalitis during hospitalization, as well as a follow-up of the sequelae of this illness were felt to be an important aspect of the complete surveillance of this disease in the Northern Thailand area. The Department of Neuropsychiatry was particularly interested in studying the neuropsychiatric complications in this disease and we were fortunate in developing a cooperative study with the major Northern Thailand hospitals to accomplish this survey.

**PROGRESS:** Excellent cooperation was obtained from the local medical and lay community in doing this clinical survey. Therefore, we were successful in following approximately 111 confirmed cases of encephalitis in the Chiang Mai area utilizing both home interviews by field team as well as return follow-up physical examinations, including E.E.G., mental status examinations, psychometric testing and complete neurological examinations during each follow-up visit.

Auxiliary data has also been obtained on the follow-up patients by interviewing teachers and employers of the patient at the school and place of work.

Presently the study is still in the data collection phase. Some of the data collected during the acute phase of hospitalization has been partially analyzed. It is planned that the complete analysis of the data will begin during the latter part of this fiscal year. The following is a breakdown of the progress made during this fiscal year in each of the work areas of the project.

#### Physical and Neurological Examinations

##### Acute Illness:

During the fiscal year under consideration in this report, 195 cases of suspected encephalitis were admitted to the four general hospitals cooperating in the study (Chiang Mai University Medical Center—79; McCormick Hospital—60; Lamphun Provincial Hospital—23; Lampang Provincial Hospital—33). Of these 195 cases, 49 patients expired during the acute phase and 136 patients were discharged in an improved condition. All of the patients admitted in these four hospitals with the suspected diagnosis of acute encephalitis received complete physical and neurological examination by the cooperating physician investigators at the various hospitals. This examination included assessment of complete past and present history of illness, general physical examination including physical measurements and vital signs; general appearance and systems examination; neurological examination, including tests for cerebral function, meningeal irritation, cranial nerves, cerebellar function, motor system, sensory system, and reflex status. The physical and neurological examinations were done at the time of admission, two weeks after admission, and at the time of discharge on all cases of suspected acute encephalitis. All data forms were in both Thai and English, and a standardized system of recording results was adopted by all of the doctors. Approximately 1620 professional man-hours have been used to evaluate and record the findings necessary for this aspect of the survey up to this time.

##### Follow-up Data Collection:

During the follow-up phase 111 serologically confirmed cases of encephalitis were followed at intervals of one month during the first three months, two months during the next four months and three months throughout the remainder of the one year follow-up after discharge from the hospital. If the patient was discharged from either Chiang Mai University Medical Center, Lamphun Provincial Hospital, or Lampang Provincial Hospital, he received his follow-up examinations at Chiang Mai University Medical Center. If he was discharged from McCormick Hospital he would be examined by the Chief Pediatrician of McCormick Hospital during follow-up examinations. Follow-up examination includes an interval history taken by the

physician, and a repeat physical and neurological examination which is recorded on the standardized forms maintained from his hospitalization. Duplicate copies of all examinations are kept on file at the Department of Neuropsychiatry office established on the Pediatrics Wards of Chiang Mai University Medical Center.

### E.E.G.

#### Acute Illness :

An electroencephalogram was done on all admitted cases suspected of having acute encephalitis during the hospitalization period. Over 100 EEG records were done during this period and the abnormal records could be classified into five patterns.

- Pattern I: This is the largest group; this pattern was found in approximately 30% of the patients evaluated during the acute phase. The record has the slow background activity of 4-6 cycles per second, intermixed with large slow waves of higher amplitude. This pattern was seen throughout the record, but locally in some of the records.
- Pattern II: This is the second largest group. The EEG showed generalized large slow waves of very high voltage. The electrical frequency is 1 1/2 to 3 cycles per second, amplitude, 200-300 micro volts. There was asymmetry of the records in some cases. Twenty percent (20%) of the patients were found to have this type of record.
- Pattern III: There were approximately 10% showing this pattern of focal or generalized sharp wave or spike-like activity. This abnormality was mainly seen in generalized form.
- Pattern IV: Four percent (4%) of the total patients studied during the acute phase were found to have this abnormal record, which is a mixture of large slow wave and sharp wave or a spike-like activity.
- Pattern V: Five percent (5%) of the patients were classified in this group. The record has a burst of large slow waves interrupted by a flattened record.

Approximately 1/3 of the suspected cases of encephalitis showed normal EEG during the acute phase of the illness. Study numbers of all cases were correlated with the EEG patterns. Of the cases of suspected encephalitis on whom EEG were done during the acute phase, approximately 72% of those on which serologies were done showed positive titers for Japanese B. Encephalitis virus. It is clear now that the abnormal patterns in the cases of positive serology for Japanese B. virus are mainly in patterns I and II, which indicate a generalized involvement of the brain in the cases of acute encephalitis.

#### Follow-up Data Collection :

During each follow-up examination visit, an electroencephalogram is done. Results of the electroencephalographic readings are presently being ordered and analyzed. These are expected to be reported during the next fiscal year, along with other data collected during the follow-up phase.

### Mental Status Examination

#### Acute Illness :

Mental status examination was done by the Director of Suan Prung Psychiatric Hospital on all patients suspected of having acute encephalitis during their period of hospitalization. Report was made of the patient's general appearance, consciousness, speech, affect, mood, thought process, thought content, perception, memories, judgment, and insight. Most commonly found during acute illness was disorientation, apathy, lack of insight, and blocking of speech. All mental status examinations were accomplished either in the general hospital, or at Suan Prung Psychiatric Hospital.

#### Follow-up Data Collection :

Mental status examinations are done on all cases of convalescent encephalitis at Suan Prung Psychiatric Hospital by our cooperating Thai psychiatrist as part of the follow-up examination.

The results of the mental status examinations during follow-up have not been analyzed, and will be reported in the future.

#### Psychometric Testing

##### Acute Illness :

Psychometric data were collected on approximately 100 patients during the acute phase of the illness. Testing was carried out by five psychologists at the Suan Prung Hospital. Adults were administered (1) the Zung test for the measurement of depression; (2) the Bender Gestalt Visual Motor Test; (3) the Performance Sub-Tests from the WAIS; and (4) the Organic Integrity Test to measure subjects' tendency to solve problems by "immature" color matching. For children the Goodenough Draw-a-Man test was substituted for the Zung test.

General findings indicated disturbances of two main types; (1) subjects exhibited passive, hypokinetic motor activity and clouding of consciousness. This group was also negativistic, and showed regressive behavior such as crying; and (2) Hyperkinetic subjects, who showed impulsive, agitated, aggressive behavior. Self-depreciation and destructive behavior in this group was common.

#### Follow-up Data Collection :

Test scores have also been collected at the time each patient returns to the hospital for follow-up visits (6 per year): These data are still being collected.

Analysis of these data is expected to commence in June 1971.

In addition, the psychologists plan to continue collecting psychometric data on all new acute encephalitis patients admitted to the hospital during the 1971 rainy season.

#### Field Team

A field team consisting of two public health nurses and a driver visited homes, places of employment, and schools to conduct interviews to assess the post-hospitalization course of the patients in these environments. After the patients are discharged from the hospital, the field team will have completed more than 500 home visits on the patients who were discharged from the four hospitals and more than 100 visits to schools and places of employment. Signs and symptoms that were frequently reported during the early phases of follow-up by the families included irritability, memory difficulties, and tremors.

During home visits it was noted by the public health nurses that most of the patients with encephalitis came from poorer families, lived all together in small bedrooms, and sometimes do not have enough mosquito nets. Some of the cases reported that they stayed up late at night watching their farms and live-stock.

It was further reported that the encephalitis seemed to be spread over a large geographic area rather than many cases in each village. The following is a break-down, geographically, of the cases admitted to the four cooperating hospitals :

Chiang Mai Province :	60 cases, with the highest number reported from Amphur Muang, and Amphur Doi Saket.
Lamphun Province :	25 cases, the largest number coming from Amphur Muang.
Lampang Province :	25 cases, the largest number coming from Amphur Muang.
Chiang Rai Province :	2 cases.

The low number of cases reported from Chiang Rai indicates merely the way in which cases were selected for this study. The majority of cases from Chiang Rai Province were admitted to the provincial hospital in Chiang Rai, which was not one of the cooperating hospitals, and therefore the low number of cases reported in our study does not reflect the actual number of cases from this province.

At the time of discharge from the hospital, there were different recommendations to the families regarding the time to return to school or work, in an attempt to study the influence of this variable on the convalescent encephalitis patient's functioning. The effect of these different recommendations for return to school will be analyzed at the completion of the follow-up study during the next fiscal year. Data acquired from the teachers and work supervisors during visits shortly after the patients were discharged from the hospitals, revealed the following: The most frequent symptoms reported were poor school and work performance, poor memory, decreased intellect, slurring of speech, and general irritability. Further analysis of the entire body of data collected during the follow-up study in field must await completion of the year of study.

#### Laboratory Support

Serological testing including hemagglutination inhibition tests and complement fixation tests was done on blood samples drawn on patients at the time of admission and two weeks after hospitalization. Presence of Japanese Encephalitis was determined if there was a four-fold change of antibody titer in the patient's serum. There were several difficulties regarding serological confirmation, in that 20% of the cases could not be confirmed serologically because of either of the following reasons:

- (1) Failure to get paired sera due to the expiration of the patient.
- (2) Failure to get paired sera due to misunderstanding on the patient's part, and/or loss of the second sample because of the patient not following instructions.
- (3) Failure to get the first blood specimen early enough during the acute illness, due to late admission of the patient.
- (4) Collection of the second blood specimen too early, rather than allowing two weeks interval between the first and second blood-letting.

Despite difficulties in the collection of the sera, 84% of the sera sent for serology testing were positive for Japanese Encephalitis. From these results we may assume: (a) clinical diagnoses made by the physicians were quite accurate and reliable, and (b) for the patients whose sera did not show a four-fold change in antibody titer, there may have been other possible agents causing their encephalitis syndromes.

Besides serological testing, other laboratory diagnostic procedures were available to this study through the services of the Department of Virology at SEATO Medical Research Laboratory. Virus isolation from brain specimens of patients who had expired during the acute phase were attempted, although none were isolated. The negative results of these specimens probably were due to technical errors in collection, storage, and transportation of the specimens. Since the viremia stage in man is less than a day or two the virus probably had already died by the time patient expired.

#### Supervision and Coordination During Data Collection Phase

Supervision of the entire project was carried out by the Department of Neuropsychiatry, including Major Marvin H. Firestone, Chief of the Department; Dr. Phon Sangsingkeo, Special Consultant to the SEATO Medical Research Laboratory and Dr. Pricha Singharaj, Public Health Physician in the Department of Neuropsychiatry. Supervision and coordination were accomplished by spending alternate periods of time in the Chiang Mai area, making arrangements for the study and refining the data collection procedures in the hospitals and field. Time requirements of the supervisors included a total of approximately 2,000 professional man-hours during the one year. A full-time secretary-clerk in the office at Chiang Mai University Medical Center was utilized for secretarial services in all aspects of the project.

**SUMMARY:** A clinical survey of the cases of Japanese Encephalitis who presented for treatment to four large general hospitals and one large psychiatric hospital in the Chiang Mai valley during the 1970 epidemic is being accomplished. This study included hospitalization and a projected one-year follow-up study of the convalescent phase. Facilities and staff of the cooperating hospitals were utilized to accomplish both aspects of the study. One hundred and ninety-five patients ranging from age 1-69 years were studied during the acute hospitalization period, and 111 cases of confirmed Japanese Encephalitis are being followed for a one-year period at home, school, and work; as well as with repeat medical and psychological examinations. Some of the findings during the acute phase and early convalescent phase of the illness are reported. The remainder of the data will be analyzed during the next fiscal year, and reported in the near future.