Clinical and Pathological Features

CALVIN M. KUNIN, M.D., and TOM D. Y. CHIN, M.D.

CLINICAL data on the 1954 outbreak of encephalitis in Texas were obtained from the 373 cases investigated by the epidemiological team, as well as from the series of 20 cases studied more extensively by Kunin and a retrospective study of 10 known fatal cases. Findings from three autopsies also were used.

Isolation of St. Louis encephalitis virus from the brain of a fatal case and from two pools of *Culex quinquefasciatus* mosquitoes, as well as confirmatory serologic evidence, led to the conclusion that Hidalgo County was experiencing an outbreak of St. Louis encephalitis, probably the largest since the St. Louis epidemic of 1933 (*1*).

Study Methods

Early in the investigation of this epidemic it became obvious that a careful clinical evaluation of the encephalitic syndrome was imperative, but it was necessary to limit the study because of the shortage of qualified investigators. A group of hospitalized patients considered fairly representative of the more seriously ill was selected. In addition, home visits were made for followup of these patients and to investigate those whose illness was less severe.

Selection of the group chosen for intensive study was based on availability of data regarding pre-encephalitic illness, hospital course, temperature curve, and cerebrospinal fluid, and data from hemogram and other studies. To facilitate communication and followup, Anglo-Americans (as differentiated from Latin-Americans) were selected, as far as possible.

The patients were visited during varying phases of their illness, usually during the acute stage and again 5 to 6 weeks later. Each was given a general physical examination, and a detailed neurological examination with special attention paid to mental status. Discussions were held with a number of key physicians in the area, who together had personally seen more than 300 cases. Their clinical impressions were essentially identical.

In the main, data from 373 epidemiological forms were obtained by lay investigators seeking information at offices of busy local physicians. Cases were accepted as encephalitis if they had been diagnosed as such by the physicians, and no attempt was made to subject these diagnoses to critical scrutiny. The data from these forms were reviewed with this in mind.

An acute and a convalescent blood specimen was drawn on each patient and sent to the bureau of laboratories, Texas State Department of Health. Of the 20 individuals who were subjected to particularly careful investigation, there was serologic information on 12. For 11 of these, a fourfold or greater rise in complement fixing antibody titer to St. Louis encephalitis was demonstrated by the Texas laboratory. A few of these were studied at the Virus and Rickettsia Laboratory, Communicable Disease Center, Montgomery, Ala., with essentially identical findings. The virus of St. Louis encephalitis was isolated from the brain of a fatal case.

Dr. Kunin was formerly with the Communicable Disease Center of the Public Health Service, on assignment to the University of Michigan School of Public Health, Ann Arbor. He is now assistant resident physician at Peter Bent Brigham Hospital, Boston, Mass. Dr. Chin is assistant chief of the Kansas City Field Station, Kans., Communicable Disease Center.

Results

The disease in the Lower Rio Grande Valley, colloquially termed "sleeping sickness," was an acute febrile illness characterized by severe headache, fever, and stupor, with signs of meningeal irritation. The course was self-limited and left few aftereffects. The morbidity was high, particularly in older age groups, but no age was spared. There were 10 deaths attributed to encephalitis. The sex distribution showed a slight preponderance of females.

Characteristically, the onset was relatively abrupt, with fever, severe generalized headache, malaise, nausea, and vomiting. Encephalitic symptoms, predominantly disorientation, irritability, and stupor, began during the first or second day of illness and persisted somewhat longer than the fever. In the more severe cases the delirious state lasted for many weeks.

Data on the relative frequency of the acute complaints show that among 342 cases, 94 percent had fever, 84 percent had headache, and 61 percent, stiff neck. Forty-seven percent experienced vomiting, 46 percent nausea, and 46 percent, muscle pain. Muscle weakness, usually of a generalized nature, was reported in 32 percent of the cases and frequently persisted for many weeks. Twenty-five percent complained of sore throat, 16 percent of constipation, and 12 percent of diarrhea. The distribution of complaints was generally the same for all ages.

On examination, the patients appeared acutely ill; nuchal rigidity and positive Kernig and Brudzinski signs were frequently demonstrated. The diagnosis was often confused with anterior poliomyelitis, in which muscle tenderness and increased resistance to passive motion in the back and hamstrings are also frequently observed. The general physical examination did not reveal any abnormalities in other organ systems.

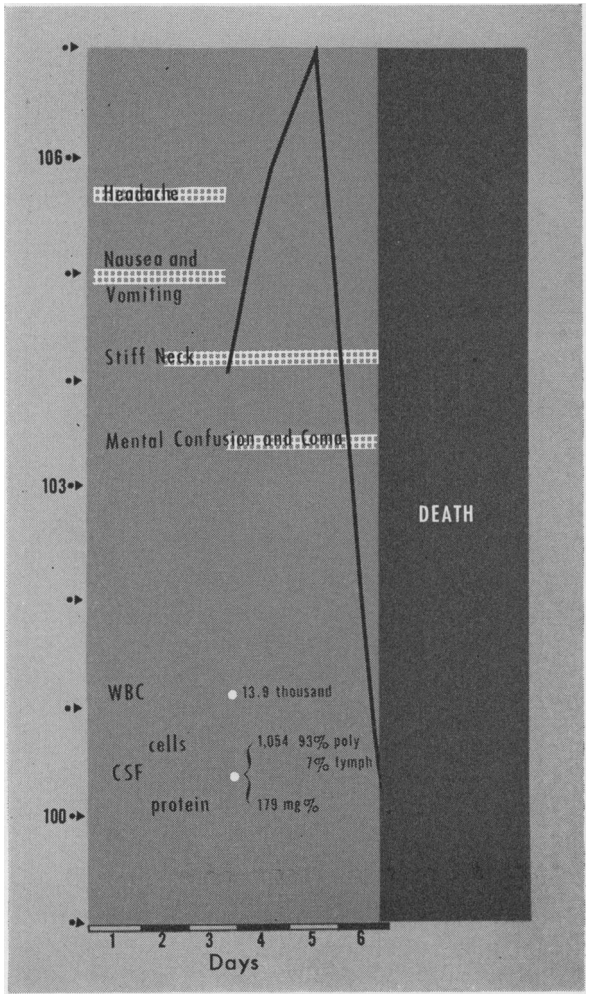
Most profoundly disturbed were the highly integrated functions of the cerebral cortex.

Summary of clinical data for 10 fatal cases of encephalitis in the Lower Rio Grande Valley, Tex.

Patient	Age	Sex	Ethnic group	Days ill	Maximum temperature	Cerebrospinal fluid		White blood count per cu. mm.	Underlying condition
						Cells	Protein (mg. percent)		
R. A.[1]	58	M	Anglo-American	5½	107° F.	[2] 1,054	179	13,950	Hypertension, arteriosclerosis, hepatic cirrhosis.
A. H.	68	F	do	9	105° F.	[2] 47	144	10,600	Asthma.
C. H.	68	F	do	18	101.6° F.	[2] 647	99	19,600	Asthma, bronchitis. Head injury in auto accident 1 year prior to death.
A. M.	60	F	Latin-American	7	105° F.	[3] 183	76	8,500	2-week diarrhea.
R. M.	89	F	Anglo-American	4	104° F.			10,000	Arthritis (senile).
M. H.	83	F	do	8	102° F.			6,100	Hypertension, azotemia, arteriosclerosis, on digitalis, terminal pneumonia.
P. C.	43	F	Latin-American	17	102.5° F.	[2] 37	([4])	4,800	None.
L. L.	80	F	Anglo-American	7	103.4° F.			10,800	Congestive heart failure, arteriosclerotic heart disease, bronchopneumonia.
M. P.	9	M	do	4	103° F.	[5] 150	50	9,000	None.
E. E.	9 mos.	F	Latin-American	3	Febrile	[2] 52		18,600	Mother had pulmonary TB and in contact with child during and prior to illness.

[1] St. Louis virus isolated.
[2] Mostly polymorphonuclear.
[3] Equal number of polymorphonuclear leukocytes and lymphocytes.
[4] Pandy test negative.
[5] Mostly lymphocytes.

Figure 1. The course of a fatal case from which St. Louis encephalitis virus was isolated.



This took the form of disorientation, stupor, and coma. At the onset of the encephalitis course, many of the more severely ill patients were agitated and difficult to manage. Within a few days the effect became bland, faces expressionless but not rigid. A number of these patients demonstrated poor general knowledge, defects in recall of recent events, and poor orientation to time, place, and person. There was no evidence of specific cerebellar damage, no muscular rigidity or nystagmus. The gait was unsteady, but the Romberg test was negative. There were no reports of oculogyric crises, Parkinsonism, or athetosis. Paralysis was rarely seen and no sensory changes could be detected. Frequently during the acute illness and persisting for at least a number of weeks during convalescence, a fine intention tremor of both hands could be demonstrated. There was no wasting nor were there any trophic changes.

The febrile course usually persisted for 3 to 7 days and generally cleared by lysis, with the maximum temperature usually reached by the second to third day. Temperature data on 260 patients indicate that more than half had a maximum of 103° F., while about 10 percent had a temperature over 105° F. A few of the more seriously ill patients, usually in the older age group, had a more prolonged illness, with a low-grade fever persisting 2 to 3 weeks. The younger patients generally had higher temperatures with shorter courses.

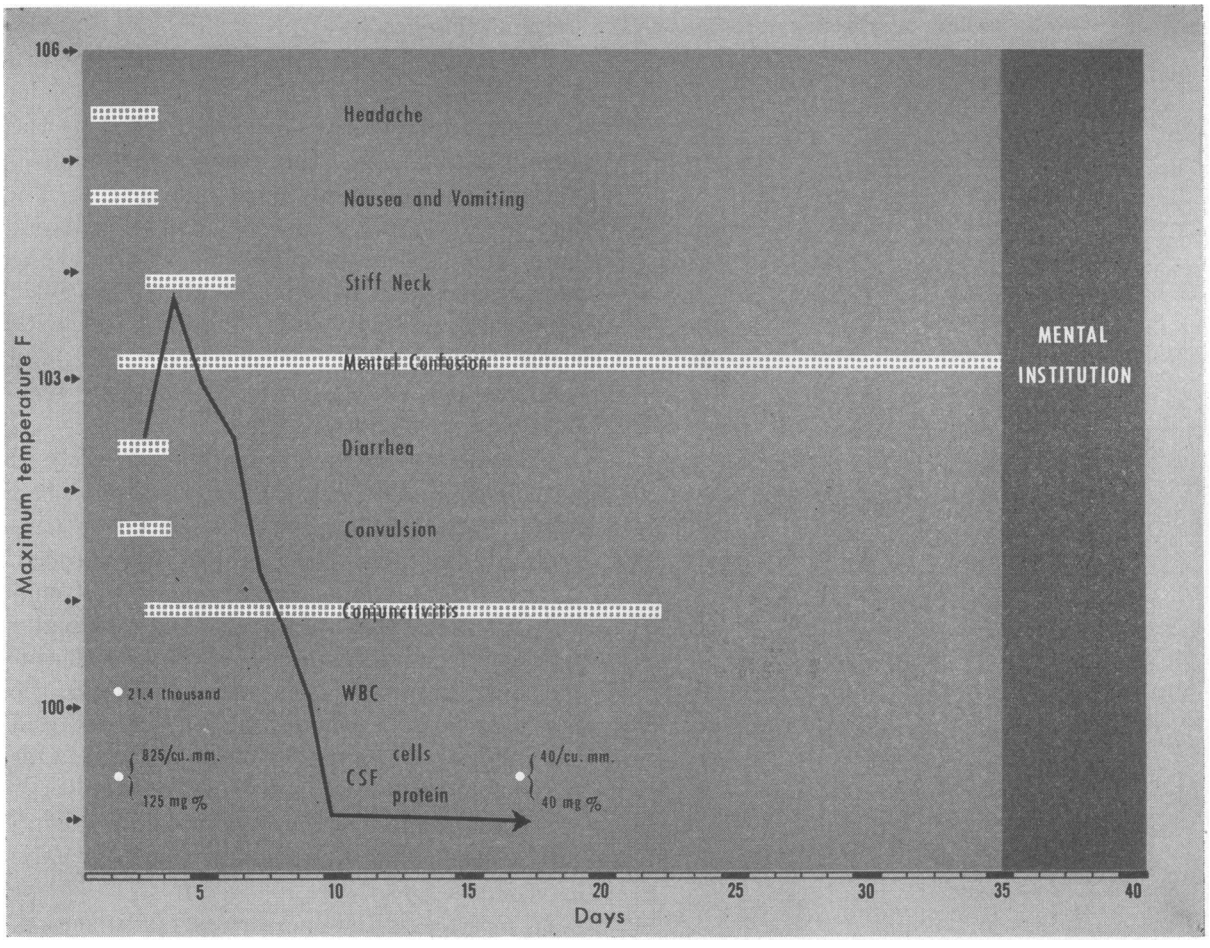
Convulsions occurred in the more severely ill patients, in most cases after the fever had begun to lyse. They were described as generalized and were seen in all age groups. A few infants demonstrated grand mal convulsions at the onset of illness when maximally febrile. In adults and older children with convulsions, the disease was more prolonged, the neurological damage was more pronounced, and the residual effects were more persistent. One patient (B. S.) apparently suffered irreversible brain damage and was placed in a mental institution. The others had surprisingly little aftereffects.

In most cases the course was fairly benign. Many had only a brief febrile illness with headache which lasted a few days. Upon recovery, the patient suffered no apparent aftereffects. A smaller number of patients developed a more progressive illness as described above, and an even smaller group developed full-blown encephalitis. Finally, there were the few critically ill patients with profound deliriums. Among those of this group who survived, the paucity of residual effects was remarkable. Observing the acute phase of the illness, one could not predict the outcome in terms of aftereffects to be seen 5 to 6 weeks later.

Ten persons died (see table), 8 females and 2 males. Eight had passed 40 years of age; 6 were 60 years of age or older. Most of the older patients also had degenerative diseases such as hypertension or arteriosclerosis, and two were asthmatic. Only 2 were ill longer than 2 weeks.

The course of the acute phase of illness is graphically portrayed for 5 hospitalized indi-

Figure 2. The course of a severe case with aftereffects.



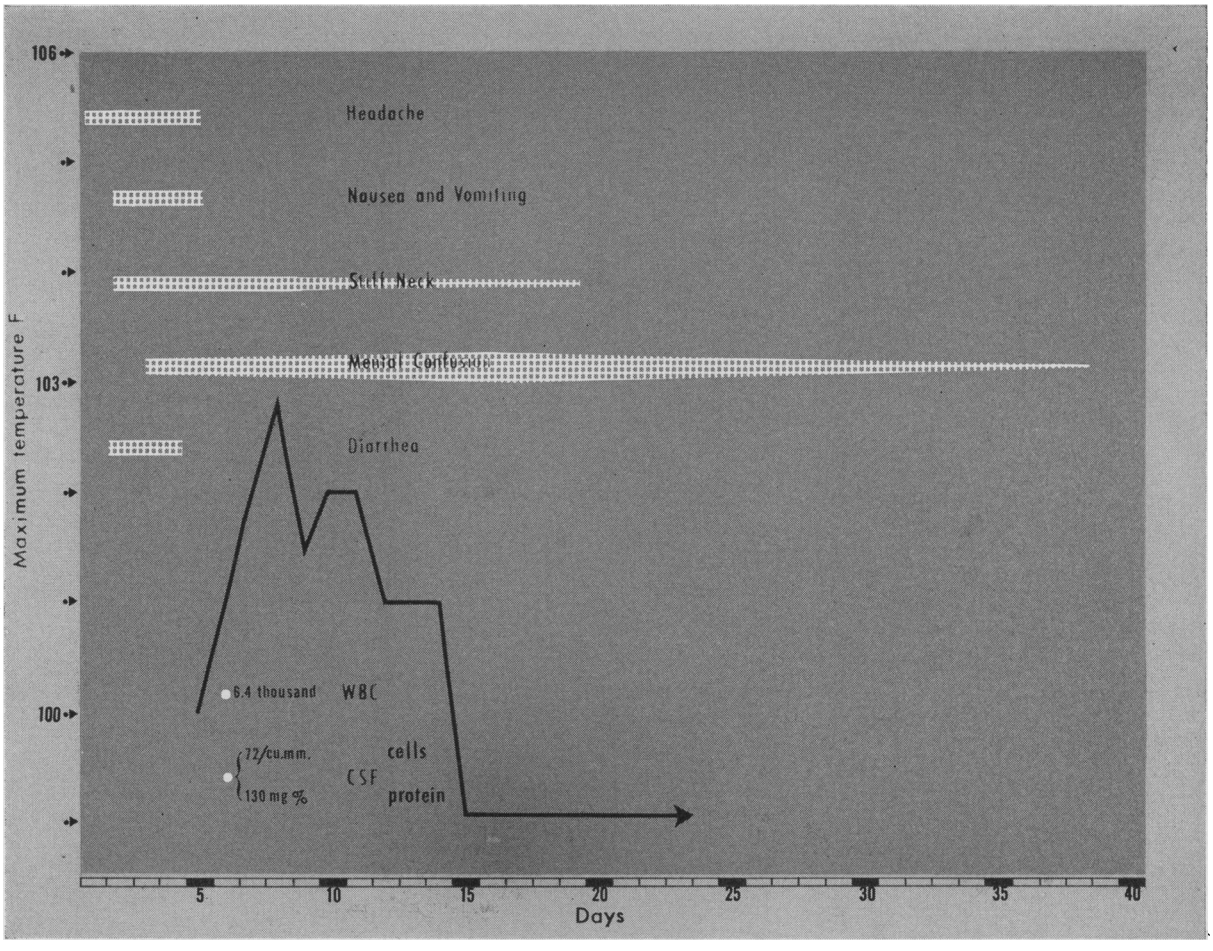
viduals. Case R. A. (fig. 1) was the patient from whom St. Louis virus was isolated. The course was quite fulminant and lasted but 5½ days. Case B. S. (fig. 2) was the most severely ill of those patients who survived. The period of mental confusion was far longer than that seen in other patients. Figures 3, 4, and 5 illustrate the more usual clinical course of severely ill patients who, after recovery from the febrile, confused, early phase of the illness, appeared to be quite well except for weakness and tremors. Case C. A. (fig. 5) was the only individual seen by the investigators who had a paralytic component, a transient left facial weakness.

Clinical Laboratory Findings

For most of the patients, laboratory studies consisted of a single test performed in the acute phase of the illness. The white blood count was reported in 118 cases. Leukocytosis was moderate, with almost half of the cases exhibiting counts greater than 10,000 cells per cu. mm., but only 7 (about 6 percent) showing counts over 20,000 cells per cu. mm. Two patients had less than 4,000 cells per cu. mm. In general, the ranges were evenly divided among all age groups, the younger patients tending to have a greater leukocytosis. There was no breakdown for differential counts.

Spinal fluid data were reported in 110 cases. Eighty percent demonstrated a pleocytosis greater than 10 cells per cu. mm. in the cerebrospinal fluid (CSF). The majority of patients had counts in the range of 50–250 cells per cu. mm. Only 3, or slightly more than 2 percent, had a cell count greater than 500 per cu. mm. In general, the younger patients had a greater pleocytosis than those in the older age groups. There was no direct correlation between severity of illness and CSF cell count. Differential

Figure 3. The course of a severe case with good recovery.



counts reported in 40 specimens performed during the acute illness demonstrated that polymorphonuclear cells predominated. In a few individuals tapped later in the course, the cells generally were mononuclear.

The CSF protein as determined in 92 patients was elevated above 40 mg. percent in about 80 percent of cases. In a few, values over 200 mg. percent were recorded.

Neuropathological Findings

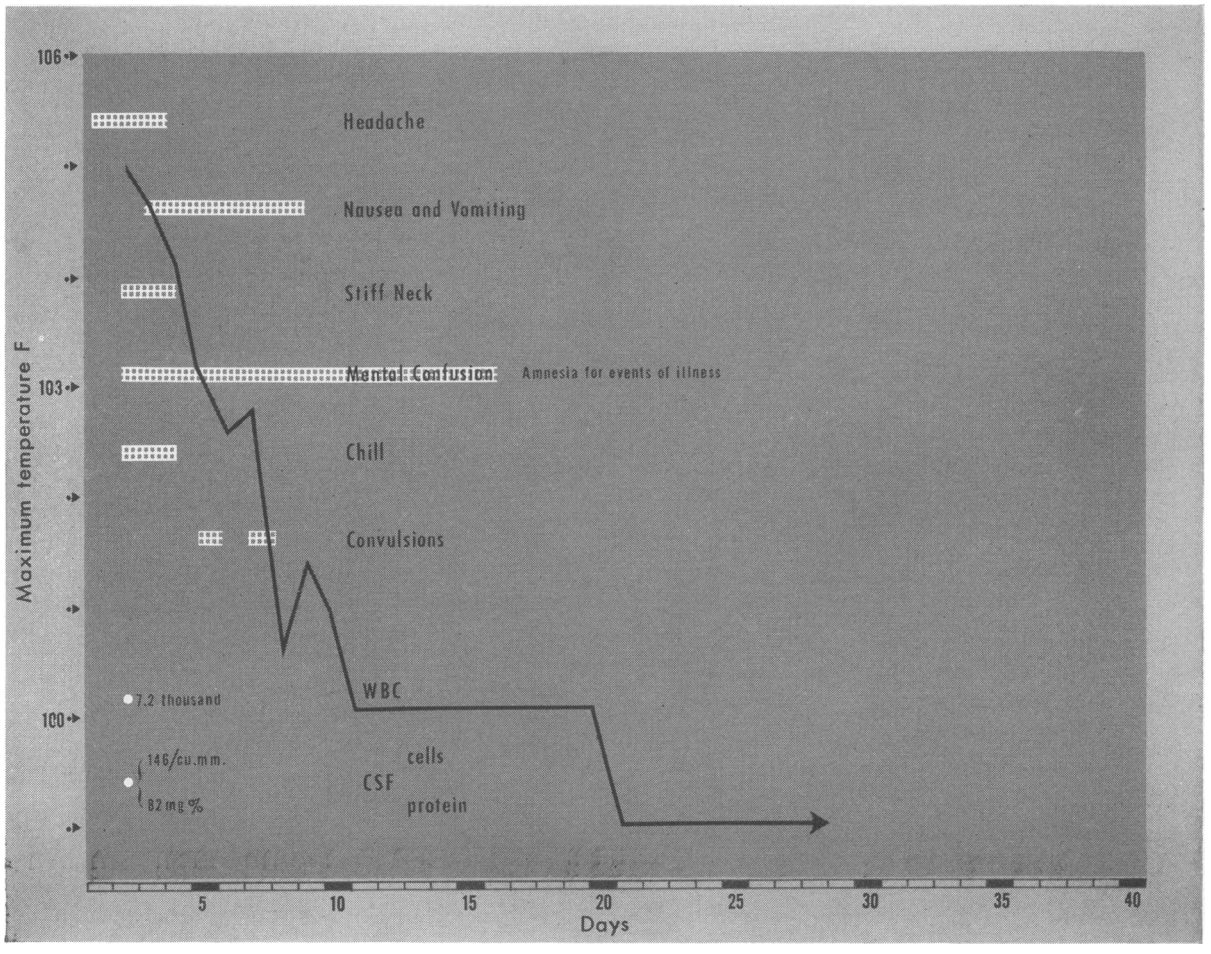
Pathological examination was performed on the brain tissue of 3 fatal cases, including 1 from which the virus was isolated.

Gross findings were reported normal in one case autopsied by a local physician. In the others the brain tissue was diffusely edematous and hyperemic. The meninges were thickened and the meningeal vessels were congested. On sectioning, petechial hemorrhages and discoloration were found in the gray matter. The tissue was soft and pliable.

On microscopic examination, the leptomeninges were thickened and the blood vessels congested and dilated. The histological changes in the brain consisted of perivascular infiltration, proliferation of microglial cells, and neuronal degeneration. These lesions were observed in all parts of the brain, in the white matter as well as in the gray matter, with the basal structures most intensely affected. Extravasation of blood into perivascular spaces and petechial hemorrhages into the brain substance were also encountered.

Microglial proliferations were frequently seen, although they were not so common as perivascular infiltrations. These lesions appeared as focal collections of inflammatory cells, the bulk of which consisted primarily of proliferated microglial cells. Under low-power

Figure 4. A severe case in a Mexican farm laborer (bracero) with good recovery, exhibiting amnesia for the events of his illness.



magnification, these foci appeared as glial nodules. In the areas with more intense cellular infiltration, neuronophagia could be noted. Several states of degeneration were observed in nerve cells, varying from mild cytoplasmic changes to complete cellular destruction.

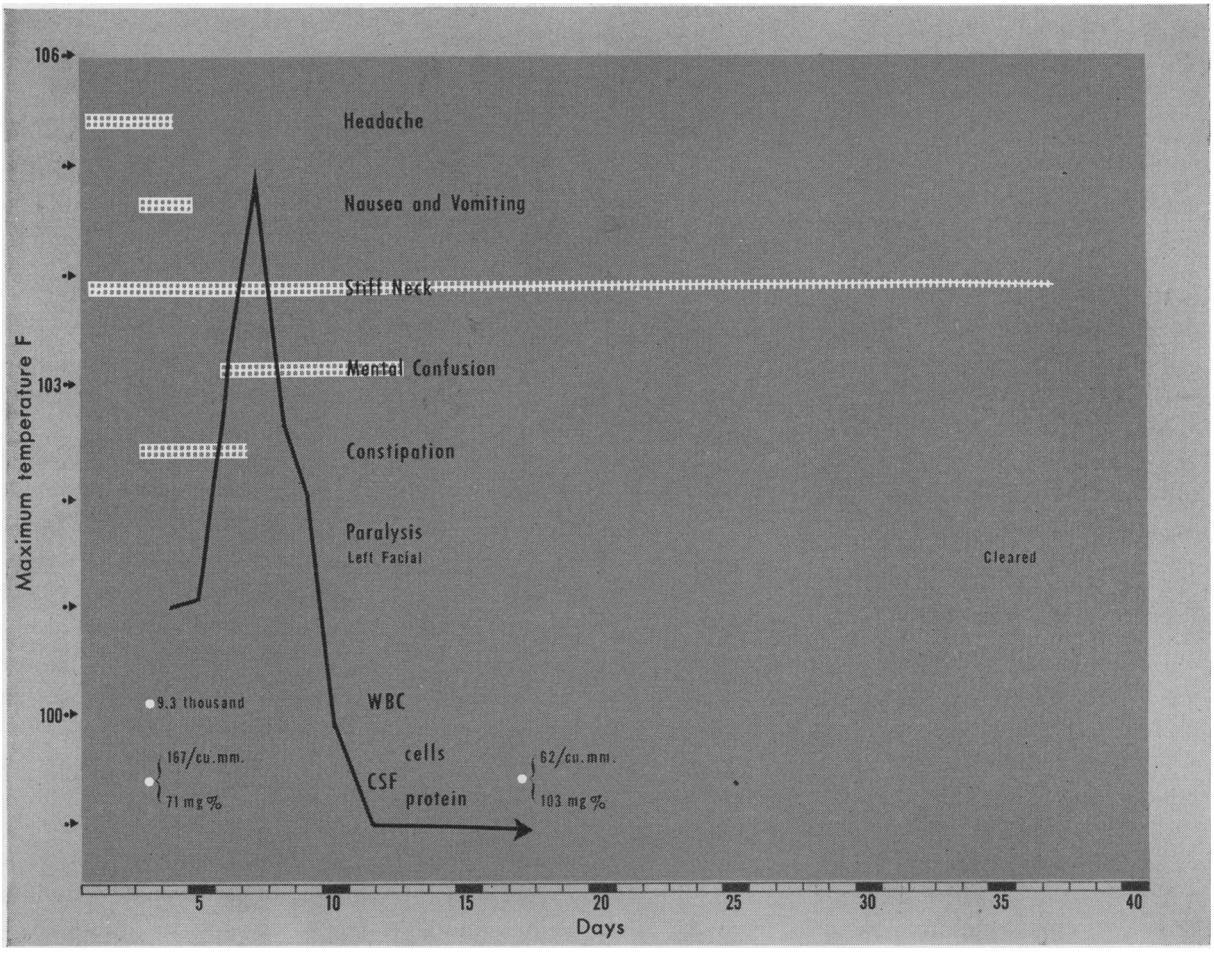
Discussion

On a clinical basis, this epidemic may be described as a generally mild, occasionally severe encephalitis with a high morbidity, a low mortality, and an approximately equal sex ratio. Remarkable features are acute onset with the development of high fever, usually clearing by lysis, severe headache, and striking recoveries in severely ill patients after prolonged coma and convulsions. This study was confined to a 5- to 6-week followup after onset. Personality changes during the acute illness were profound in a number of individuals but the prognosis for most should be good (*2*).

Although in the fatal cases lesions were distributed throughout the brain and were particularly noticeable in the basal structures, clinically, the higher integrative functions of the central nervous system were most profoundly disturbed. Paralysis, ocular palsies, and discrete localization of neurological signs were infrequent. The dulling of effect and intellectual functions, generalized weakness, and bilateral tremor of the hands were pronounced features in the convalescent patient.

The laboratory findings of a moderate pleocytosis and an elevated spinal fluid protein were typical of aseptic meningitis, and pathologically the lesions were consistent with those of the arthropod-borne encephalitides (*3*, *4*).

Figure 5. The course of a moderately severe case exhibiting transient left facial weakness.



The findings were not diagnostic of St. Louis encephalitis itself and could not be used as criteria to differentiate it from other encephalitides.

Most of the patients who died had some form of chronic disease which probably contributed to death, and most of them were over 50 years of age. Clinically, this epidemic displayed many of the features of St. Louis encephalitis, and this diagnosis is entirely compatible with the findings.

Summary

The description of the clinical and pathological features of the 1954 outbreak of encephalitis in the Hidalgo area of Texas is based on 20 cases studied by Kunin, 373 cases reported on clinical-epidemiological forms, and results of 3 autopsies. It is concluded that the clinical and pathological features of this epidemic are similar to those previously described for St. Louis encephalitis.

REFERENCES

(*1*) U. S. Public Health Service: Report of the St. Louis outbreak of encephalitis. Pub. Health Bull. No. 214. Washington, D. C., U. S. Government Printing Office, 1935.

(*2*) Finley, K. H., Longshore, W. A., Jr., Palmer, R. J., Cooke, R. E., and Riggs, N.: Western equine and St. Louis encephalitis. Preliminary report of a clinical follow-up study in California. Neurology 5: 223–235, April 1955.

(*3*) Wolf, A.: The pathology of some viral encephalitides. *In* The pathogenesis and pathology of viral diseases, edited by J. G. Kidd. New York, N. Y., Columbia University Press, 1950, ch. 14, pp. 194–213.

(*4*) Finley, K. H., and Hollister, A. C. J.: Western equine and St. Louis encephalomyelitis—The distribution and histological nature of central nervous system lesions. California Med. 74: 225–229, April 1951.