Infectious Encephalitis In Colorado

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BETWEEN May 1, 1956, and December 31, 1957, 258 cases of infectious encephalitis in Colorado were reported to us by physicians, hospital personnel, local health departments, and the Colorado State Department of Public Health. For most of these cases, it was necessary for us to rely on the clinical judgment of those making the diagnosis; since the acute phase of the illness had generally passed by the time the case was reported, laboratory diagnosis was not possible. Infectious encephalitis is generally defined as an acute disease process in which the patient exhibits typical signs and symptoms of central nervous system involvement (headache, fever, stiff neck and back, drowsiness, and spinal fluid pleocytosis) with a micro-organism as the presumed etiological agent.

This paper presents certain epidemiological aspects of this syndrome observed in the above-mentioned cases and compares some of these aspects as they differed according to the etiological agent involved.

Methods

Attempts were made to gather basic epidemiological information on all cases as they were reported. This information included, among other things, geographic, time, age, and sex data for each case. At the end of the 20-month period these isolated bits of information were compiled to demonstrate the geographic, time, age, and sex distributions of the cases.

Serum specimens were collected from patients when possible. In general, these specimens were paired, with one specimen taken early in the course of the disease (acute phase) and the second taken 3 to 6 weeks later, during convalescence. Occasionally, only convalescent-phase specimens could be collected.

All specimens were tested with the hemagglutination-inhibition (HAI) test for antibodies against St. Louis encephalitis (SLE) and western encephalitis (WE). Most of the specimens were also tested with the serum neutralization (SN) test for antibodies against the same diseases. If sufficient sample remained it was tested with the complement fixation (CF) test for antibodies against mumps, lymphocytic choriomeningitis (LCM), and eastern encephalitis (EE) in addition to SLE and WE. (All CF tests were performed by the Communicable Disease Center, Virus and Rickettsia Laboratory, Chamblee, Ga.) The three poliomyelitis types were added to the CF battery in 1957. Also in 1957, convalescent-phase specimens from 27 patients which showed insignificant antibody titers in all the above tests were subjected to the SN test for ECHO viruses, types 2, 4, 6, and 9, and serums from 18 patients were subjected to the SN test for Colorado tick fever. (Tests for ECHO viruses were performed by the department of pediatrics, University of Colorado Medical Center, Denver, Colo. For Colorado tick fever, tests were performed by the Rocky Mountain Laboratory, Hamilton, Mont.)

A case was considered serologically "confirmed" if a fourfold rise in HAI or CF titer or tenfold rise in neutralization index could be demonstrated in paired specimens. A case was considered serologically "suggestive" when a CF titer of 1:8 or HAI titer of 1:80 was present but a rise in titer could not be demonstrated. The cases were then categorized ac-

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Table 1. Etiology of 258 cases reported as infectious encephalitis in Colorado between May 1, 1956, and December 31, 1957

Classification	Method of diagnosis	Number of cases
St. Louis encephalitis	Serologic	21
Probable St. Louis encephalitis.	do	27
Western encephalitis	do	20
Probable western encephalitis.	do	5
Mumps	do	1
Mumps	Clinical	23
Measles	do	1
Influenza	do	4
Influenza	Serologic	1
Influenza	Virus isolation	1
Postvaccinal encephalitis	Clinical	1
Poliomyelitis type 1	Serologic	2
Poliomyelitis type 2	do	1
Colorado tick fever	do	1
Etiology unknown		149

cording to etiology by month of onset and age and sex of the patient.

Results

Study revealed that the 258 cases were, for the most part, roughly distributed in proportion to population density throughout Colorado. There were two exceptions to this rule. One was Grand Junction in Mesa County, and the other, the plains area in eastern Colorado. An unusually high attack rate was seen in both of these places as a result of localized outbreaks of SLE in the summer of 1956. Cases were reported in each of the 20 months under discussion. The majority of the cases, however, are grouped together into two separate time periods: the late summer and early fall months of 1956 and the same period in 1957.

Each age group was involved, with the youngest patient 6 days of age and the oldest 82 years. There was, however, a marked preponderance of cases among people under 20 years of age, particularly among those under 10.

The etiological agent was defined by laboratory or clinical means in 109 of the 258 cases (table 1). The arthropod-borne diseases, SLE and WE, accounted for 67.0 percent of the cases in which the etiology is known, while mumps accounted for 22.0 percent. Influenza was next in line, followed by poliomyelitis, measles, Colorado tick fever, and postvaccinal encephalitis.

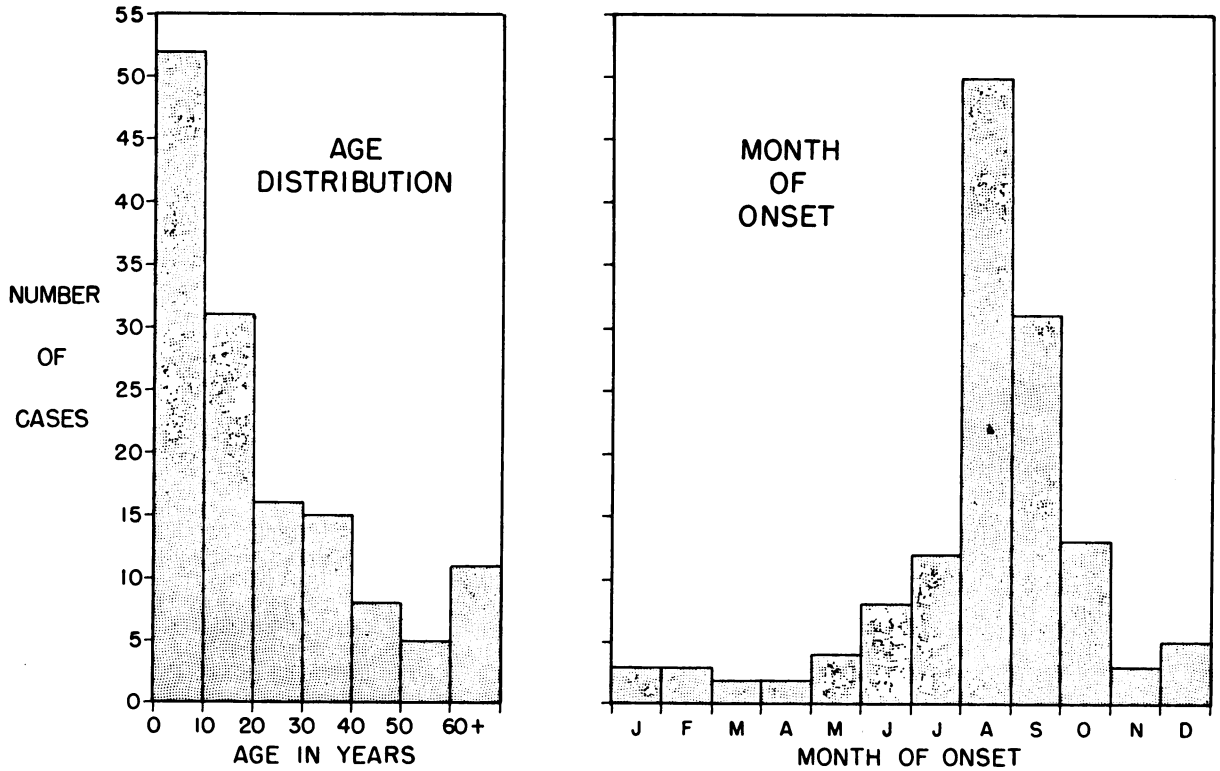
An effort was made to exclude cases of nonparalytic poliomyelitis from the study. The three cases that are included were originally reported as infectious encephalitis, and it was only on subsequent serologic examination that the true etiology of the disease became known. On the other hand, two cases which were originally reported as nonparalytic poliomyelitis were subsequently found, on serologic exami-

Table 2. Results of serologic tests for various etiological agents of infectious encephalitis

Disease	Ratio of cases [1] to paired specimens tested			Percent positive of those tested
	1956	1957	Total	
St. Louis encephalitis	43/61	5/64	48/125	38. 4
Western encephalitis	3/61	22/64	25/125	20. 0
Mumps	0/45	1/46	1/91	1. 1
Lymphocytic choriomeningitis	0/45	0/46	0/91	0
Eastern encephalitis	0/45	0/46	0/91	0
Poliomyelitis type 1	0/0	2/46	2/46	4. 4
Poliomyelitis type 2	0/0	1/46	1/46	2. 2
Poliomyelitis type 3	0/0	0/46	0/46	0
Asian influenza	0/0	1/2	1/2	50. 0
Colorado tick fever	0/0	1/18	1/18	5. 6
Results conclusive	46/61	33/64	79/125	63. 2
Results inconclusive	15/61	31/64	46/125	36. 8
Total	61/61	64/64	125/125	

[1] Includes "confirmed" and "suggestive" cases.

Figure 1. Cases of unknown etiology reported as infectious encephalitis, Colorado, July 1, 1956–December 31, 1957.

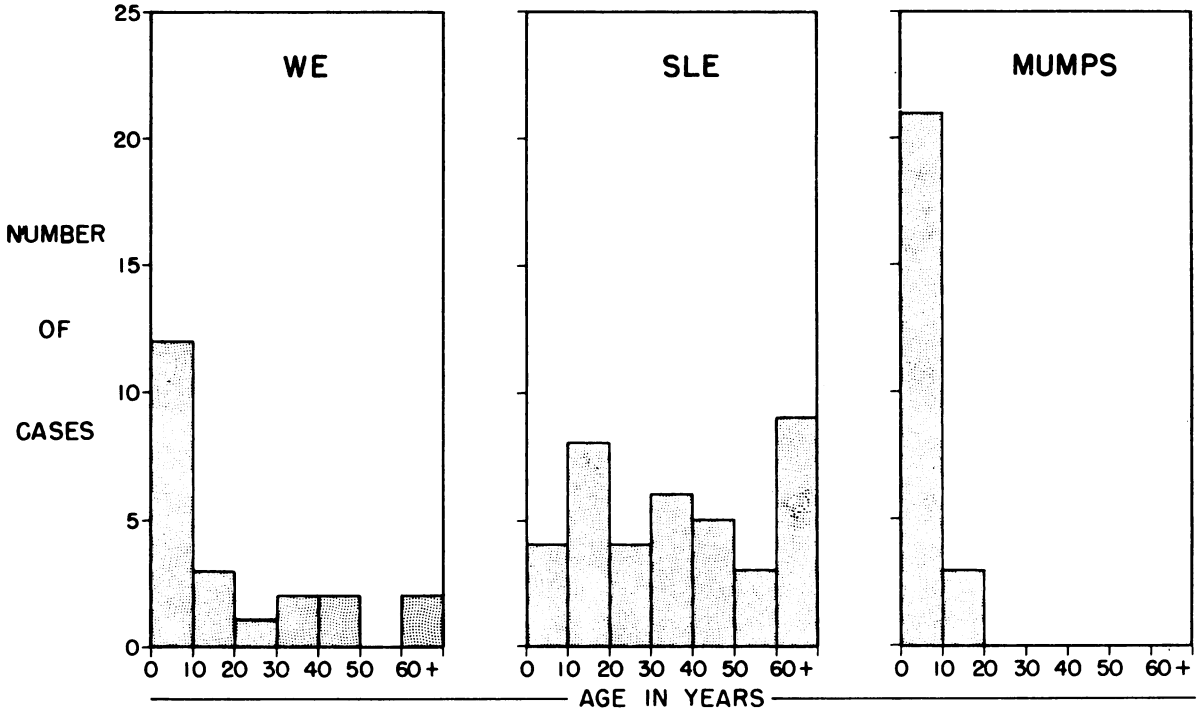


nation, to be WE. The largest group, unfortunately, is that in which the etiological agent is unknown. This group is composed of 149 cases, or 57.8 percent of the total number.

Results of the serologic tests can be seen in table 2. The largest number of specimens (125) were tested for antibodies against SLE and WE. These two diseases, in order, were responsible for the largest numbers of serologically confirmed and suggestive cases. Fifty percent of those tested for Asian influenza were confirmed to give the highest ratio of cases to paired specimens tested in this series. However, this involved serum specimens from only two individuals. SLE was next highest with 38.4 percent, followed by WE with 20.0 percent. Smaller percentages were noted for the other diseases mentioned previously. Low-level antibody titers against various types of ECHO virus were found to be present in 8 of the 27 (29.6 percent) convalescent-phase specimens tested. None of the specimens had antibodies against type 4, two had antibodies against type 2, six had antibodies against type 6, and five had antibodies against type 9. Two specimens had antibodies against types 6 and 9, one against types 2 and 9, and one against types 2, 6, and 9. No attempt will be made to interpret these results since it is not known whether any of the serums underwent a rise in titer. Attempts at interpretation would be made still more hazardous by the lack of knowledge concerning the presence of such antibodies among the general population in this area. One of the 18 (5.6 percent) tested for Colorado tick fever was considered "confirmed" on the basis of an 18-fold rise in neutralizing titer. Moderately high titers were demonstrable in the serum of three other patients, but, again, since there was no significant rise in titer, no attempt will be made at interpretation.

As noted previously, the largest group studied was that in which the etiology was unknown. Age distribution and distribution by month of onset for that group are given in figure 1. The seasonal distribution for the next three largest groups, SLE, WE, and mumps, may be seen in figure 2, and the age distribution

Figure 2. Seasonal distribution of western encephalitis, St. Louis encephalitis, and mumps encephalitis, Colorado, May 1, 1956–December 31, 1957.



in figure 3. The age distribution was somewhat alike for WE, mumps, and cases of unknown etiology in that the disease was primarily in individuals under 20 years of age. SLE showed fairly even case distribution among all age groups with only a slightly larger number of cases among older people. The seasonal distribution of cases of unknown etiology (fig. 1) looks somewhat like a composite of the distribution of SLE, WE, and mumps (fig. 2), with cases occurring in each month of the year. An increase in the number of cases starts in May, continues through June and July, and reaches a peak in August. From there it declines gradually through the month of October. WE and SLE are restricted to the late summer and early fall months, while mumps is seen in all seasons, but primarily in the spring. The sex distributions, shown below, for WE, SLE, and mumps are similar, with more males than females in each group.

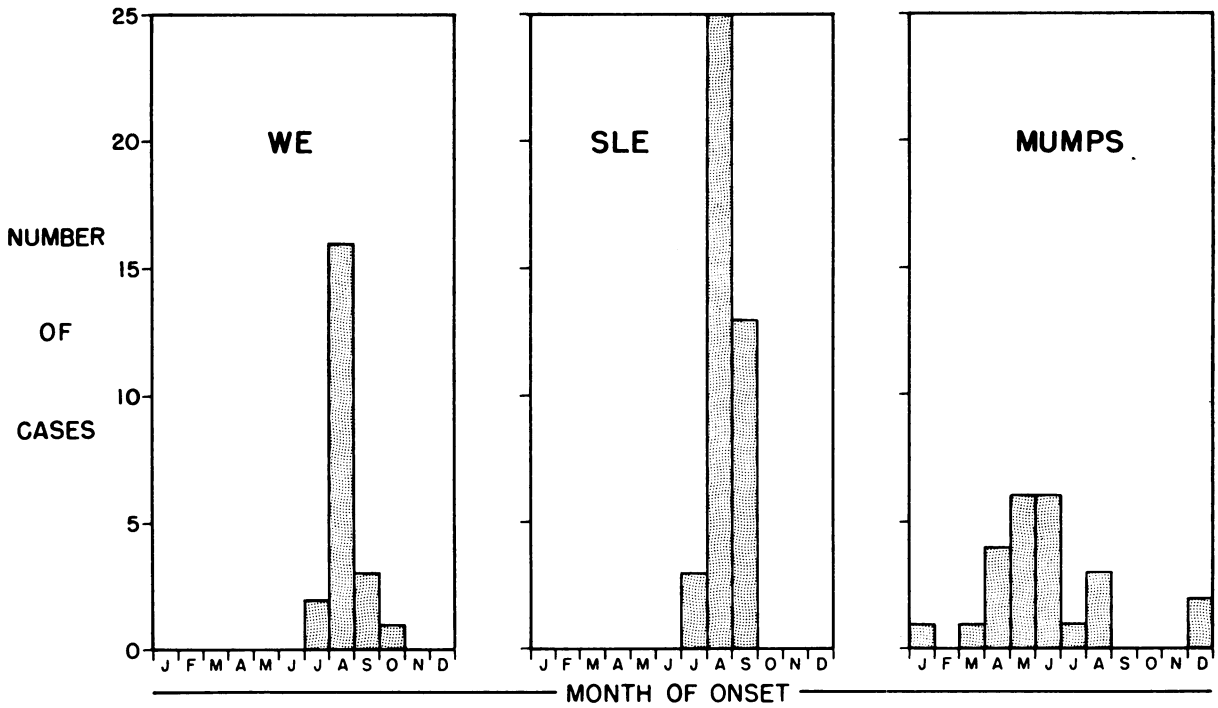
	Number of cases		
	WE	*SLE*	*Mumps*
Male	16	23	18
Female	7	19	6

There were 10 deaths among the 258 patients. One of the fatal cases, with signs and symptoms typical of encephalitis, was felt to be due to Asian strain type A influenza since the virus was cultured from a piece of lung tissue taken at autopsy. Two of the deaths were thought to be possibly due to SLE because of moderately high antibody titers in specimens taken during the acute phase. In each case the patient died before a second specimen could be obtained. Virus isolation attempts were made on a section of brain from one of the two patients, but no viruses were obtained.

Discussion

The fact that the cases of infectious encephalitis observed were distributed roughly in proportion to the human population would lead one to believe that the causative agents are widely distributed within the State. All the agents are not known, but SLE, WE, and mumps would appear to be particular problems. However, since a special effort was made to search out cases of SLE and WE, it may be that

Figure 3. Age distribution of western encephalitis, St. Louis encephalitis, and mumps encephalitis, Colorado, May 1, 1956–December 31, 1957.



the importance of these two diseases is exaggerated. It is entirely possible that an even greater problem lies hidden among those cases of unknown etiology but we have no evidence of such. It is only possible to theorize concerning the possible agents involved in that group. It would seem likely that some of the cases on which laboratory procedures were not carried out were nonparalytic poliomyelitis and WE, or were due to encephalitogenic types of ECHO or Coxsackie viruses. This assumption can be borne out to a minor degree by comparing the age distribution and epidemic curves of these cases of unknown etiology (fig. 1) with those of outbreaks of the diseases mentioned above (*1–3*). The significance of the presence of antibodies against certain types of ECHO viruses among some of these patients is not known. SLE can also be compared as far as the epidemic curve (fig. 2) is concerned, but the age distributions do not compare well (fig. 3). A number of those cases which occurred in the winter, spring, and early summer might very well have represented mumps encephalitis without clinical parotitis. It has been noted in the past that as many as 50 percent of the cases of mumps encephalitis fit into this category (*4*).

Unfortunately, many cases of encephalitis are never reported to authorities in Colorado. With more complete reporting and the submitting of specimens for testing from most of the encephalitis patients, it seems likely that mumps would become the largest etiological group, as it is in California (*5*). An additional problem is the confusion in attempting to differentiate between nonparalytic poliomyelitis and infectious encephalitis on a clinical basis. It is generally agreed among those who do a great deal of work with acute diseases of the central nervous system that the only reliable way to make such a differentiation is on the basis of laboratory findings.

Probably the most striking feature, though one that would not be unexpected, is that all cases of mumps encephalitis were seen in patients under the age of 20. While WE shows a tendency to infect people of most ages, it is obvious that this disease, like mumps, attacks more people in the younger age groups than in the middle and older age groups.

SLE tends to infect people of all ages, with a slight preference for the older age groups. The difference between mumps and SLE can be explained by the fact that mumps is a highly infectious disease, endemic in most areas of this country, which becomes epidemic whenever a sufficient number of people who are not immune are present. This means that as children are born following a mumps epidemic the stage is being set for a new epidemic several years later. As a result of these frequent epidemics most people become immune before reaching an advanced age. SLE and WE, on the other hand, while they are both endemic in Colorado (*6*), can probably be spread only by the bite of an infective mosquito (*7*). The incidence of these two diseases in a community is therefore dependent on mosquito populations and mosquito infection rates and numerous other poorly understood factors. In light of our present knowledge, the age distribution differences between SLE and WE cannot be explained.

The preponderance of male patients infected with the SLE and WE viruses could possibly be explained by the fact that men and boys in general spend more time out-of-doors and are, hence, at greater risk of exposure to infective mosquitoes. This does not, of course, hold true with infectious parotitis since both sexes are generally affected equally (*8*).

Summary

A total of 258 cases of encephalitis were brought to the attention of the authors between May 1, 1956, and December 31, 1957. There were 10 deaths in this group. Geographic, time, age, and sex distributions of the cases were noted.

The viruses of SLE, WE, and mumps were the most common causative agents. Epidemiological characteristics of these three types of encephalitis were compared.

More diagnostic work needs to be done in the field of infectious encephalitis in order better to evaluate the problem brought about by the large number of agents which can produce this syndrome.

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