Human Equine Encephalomyelitis and St. Louis Encephalitis in California, 1939-1941*

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IN previous reports [1, 2] it had been demonstrated by means of the serum neutralization tests and by recovery of the active agent itself, that the virus of western equine encephalomyelitis has been responsible for human cases of the disease in California for some time past. Antibodies against the St. Louis encephalitis have likewise been found among the population in similar geographical areas of the two central valleys of the state. Because the equine type of encephalitis has now become recognized as a clinical entity in man, the earlier study has been continued and a summary of the findings from 1939 through October, 1941, is herewith presented. Subsequent to the earlier articles, Davis,[3] Cope and Maytum,[4] and van Wagenen [5] have published on the clinical aspects of the disease, and Buss and Howitt [6] have presented a detailed study of human equine encephalomyelitis as seen in Kern County, Calif. Because the test for neutralizing antibodies has proved an aid in the differentiation of neurotropic virus diseases, the physicians are now better able to evaluate the etiology of their cases, separating those with mild encephalitis from those having non-paralytic poliomyelitis, where formerly many were reported as the latter disease.

NEUTRALIZATION TESTS

The serum neutralization test as used in this study was employed essentially in the same manner as previously described,[2] except that rabbit serum was added to the broth diluent rather than distilled water. Two dilutions of each virus were made from a 10 per cent mouse brain suspension in Ringer's solution. The weaker dilution was about 10 times, and the stronger 50 times the least amount of virus that killed 50 per cent of the mice upon titration. The serum and virus dilutions were added in equal parts, left overnight in the refrigerator, and inoculated intracerebrally into young white mice. A serum was considered positive if it neutralized both dilutions of virus, and weakly positive if it only protected against the higher dilution. Because of the many tests performed with the same technic over a long period of time, and because they were repeated on the weakly positive sera, no differentiation has been made in computing the final results. All tests showing some degree of protection have been included as positive in the tables.

Protection tests were run routinely against the St. Louis virus of encepha-

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litis (originally obtained through the courtesy of Dr. W. T. Webster of the Rockefeller Institute) and the virus of western equine encephalomyelitis, Br. strain of human origin.[1]

Table 1 gives the comparative results of the test for the years 1939, 1940, and 1941. Sera were received not only from the two central valleys of the state but a large number from the Bay Region and adjacent coastal towns. They were all from individuals having disturbances of the central nervous system, including poliomyelitis. The sera containing antibodies for the encephalitic viruses were from residents of either the Sacramento or the San Joaquin Valley, only one being positive for the St. Louis strain in the Bay Region. However, in 1941, two sera from the coastal counties of Santa Cruz and San Mateo, south of San Francisco, were found to neutralize the St. Louis virus. Both were from adults showing neurotropic disturbances and were without contact with the inland valleys. Another serum positive for this virus was also obtained from Sonoma County north of the Bay Region. The only other protective sera have been from 6 children referred to San Francisco hospitals from the valley districts. They were all positive to the western equine strain.

The percentage of positive tests for the equine virus has fluctuated each year for the different regions as shown in Chart 1. There was an increase for Kern County during 1939 and 1940, dropping in 1941, while in Fresno County there has been a steady increase for each year. It may be of significance that more sera were positive only to the St. Louis strain from Tulare County than from the other endemic areas. The other valley counties reported many cases of encephalitis for 1940 but very few for 1941. In fact, the total number for these regions fell markedly during

TABLE 1

Results of Serum Neutralization Tests on Cases Showing Neurotropic Symptoms *

County	Positive or Negative to Virus	Number Tested	1939	Number Tested	1940	Number Tested	1941
Kern	W. equine	111	47 (42.3%)†	60	42 (70.0%)†	50	15 (30.0%)†
	W. equine alone		35 (31.5%)†	39	26 (66.6%)†		9 (18.0%)†
	St. Louis alone		5 (4.5%)†	39	0		8 (16.0%)†
	Equine and St. Louis		12 (10.8%)†	39	10 (25.6%)†		6 (12.0%)†
	Neg. to equine and St. Louis		59 (53.6%)0	60	18 (30.0%)0		27 (54.0%)0
Fresno	W. equine	42	9 (21.4%)†	25	14 (56.0%)†	36	23 (63.8%)†
	W. equine alone		8 (19.0%)†		11 (44.0%)†		12 (33.3%)†
	St. Louis alone		5 (12.1%)†		3 (12.0%)†		5 (13.8%)†
	Equine and St. Louis		1 (23.8%)†		3 (12.0%)†		11 (30.5%)†
	Neg. to equine and St. Louis		28 (66.6%)0		8 (32.0%)0		8 (22.0%)0
Tulare	W. equine	15	6 (40.0%)†	12	3 (25.0%)†	15	2 (13.3%)†
	W. equine alone		4 (26.6%)†		1 (8.3%)†		1 (6.6%)†
	St. Louis alone		2 (13.3%)†		5 (41.6%)†		8 (53.3%)†
	Equine and St. Louis		2 (13.3%)†		2 (16.5%)†		1 (6.6%)†
	Neg. to equine and St. Louis		7 (46.6%)0		4 (33.3%)0		5 (38.3%)0
Other Valley Counties	W. equine	40	13 (32.5%)†	64	31 (48.4%)†	29	8 (27.8%)†
	W. equine alone		11 (27.5%)†		23 (35.9%)†		3 (10.3%)†
	St. Louis alone		3 (7.5%)†		7 (18.9%)†		4 (13.7%)†
	Equine and St. Louis		2 (5.0%)†		8 (12.5%)†		4 (13.7%)†
	Neg. to equine and St. Louis		24 (60.0%)0		26 (40.6%)0		16 (55.1%)0
Bay Region	W. equine	54	0	50	0	40	0
	W. equine alone		0		0		0
	St. Louis alone		0		1 (2%)‡		0
	Equine and St. Louis		0		0		0
	Neg. to equine and St. Louis		54 (100%)0		49 (98.0%)0		40 (100%)0

† Sera neutralized the virus
0 Sera did not neutralize the virus
‡ Weakly positive

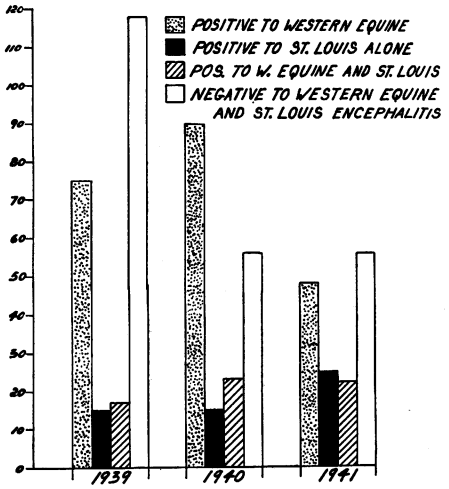


CHART 1—Comparative Incidence of Western Equine and St. Louis Encephalitis in the Central Valleys of California for 1939, 1940, and 1941 as Determined by the Serum Neutralization Tests

this year. While the figures given in the table are based on the number of sera received or on autopsy material, yet undoubtedly they do not represent all of the cases, because the blood was taken mainly from patients coming to the county hospitals, and many were probably missed.

During 1939, the number of tests that were negative to the encephalitic viruses increased for Fresno County with a corresponding decrease in those positive to the equine or the St. Louis strains. Because many cases were diagnosed as poliomyelitis and the latter virus was isolated three times from fatal cases in Fresno in 1939, it seems probable that the negative sera were mainly from poliomyelitic patients. Kern County likewise reported as many as 73 (63.7 per cent) cases of poliomyelitis during the same year.[6] In 1940, encephalitis again increased in the same areas while poliomyelitis declined.

In 1941, all types of neurotropic virus diseases had decreased. The reduction was especially noticeable for the more northerly counties in the Sacramento Valley. Only 11 sera were received, by contrast with 33 in 1940. Twenty-one (63.6 per cent) of the latter had been positive for the western equine virus, while only 5 (15.1 per cent) reacted with the St. Louis strain. Three were positive for both viruses. The decrease in encephalitis for 1941 may be interpreted as due to a change in climatic conditions, because the rains were heavy and unusually prolonged during the early months of the year and thus unfavorable for the early appearance of an insect vector.

In Table 2 are given the complete data of the neutralization tests on sera from the two central valleys for 1939, 1940, and 1941, supplemented by the records for 1937 and 1938. The total numbers represent all the cases diagnosed as some form of neurotropic virus disease, including those of poliomyelitis. Except for 1940 the percentages have remained about the same for the sera positive against the western equine virus.

TABLE 2

Total Neutralization Tests on Valley Sera against Western Equine and St. Louis Viruses

	Number Tested	*1937–38*	*Number Tested*	*1939*	*Number Tested*	*1940*	*Number Tested*	*1941*
Total W. equine	86	32 (37.0%)†	208	75 (36.0%)†	161	90 (55.9%)†	130	48 (36.9%)†
W. equine alone				58 (27.8%)†		57 (35.4%)†		25 (19.2%)†
St. Louis alone				15 (7.2%)†		15 (10.7%)†		25 (19.2%)†
St. Louis and equine	69	18 (26%)†		17 (8.1%)†		23 (16.4%)†		22 (16.9%)†
Total St. Louis	103	49 (47.5%)†		32 (15.3%)†		38 (27.1%)†		46 (35.3%)†
Negative to W. equine and St. Louis				118 (56.7%)0		56 (40.0%)0		56 (43.0%)0

† Sera neutralized the virus
0 Sera did not neutralize the virus

RECOVERY OF THE VIRUS AND MORTALITY RATES

While the differentiation of neurotropic virus diseases in California has been based largely on the results of the neutralization tests, yet findings on human autopsy material have also been available. Recovery of the viruses of both poliomyelitis and of western equine encephalomyelitis has given evidence of their presence in these localities. Previous reports have described the isolation of the latter strain from 2 human cases in 1939 [2] and later from 2 others in 1940.[6] Another human strain has been recovered in 1941 from a 9 year old boy in the Fresno General Hospital.

During 1939 the virus of poliomyelitis was obtained from 3 out of 5 fatal cases diagnosed as bulbar poliomyelitis in Fresno County and again from one in 1940. It was also isolated from the feces of 6 individuals in Kern County in 1941. It is evident therefore that this virus is endemic in these areas and that the neurotropic diseases, poliomyelitis, western equine and St. Louis encephalitis, may at times be confused, particularly the abortive or non-paralytic forms or even certain types of paralysis.

In 1937 when epidemic encephalitis first became a problem in California, there were 40 deaths out of 102 cases reported to the State Department of Public Health or a mortality of 39.1 per cent.[7] Twenty-eight of these patients were in Fresno County with 13 deaths or 42.8 per cent fatality. In 1940 the deaths had fallen considerably in the lower part of the central valleys according to the report of Dr. H. L. Wynns of the State Department of Health.[8] The rate was 18.6 per cent of 43 cases in Fresno County and 15.2 per cent of 46 cases in Kern County. On the other hand, the fatalities in the more northerly districts varied from 20 to 25 per cent.

In 1941 the death rate was lower in the valleys. Two (4 per cent) out of 50 neurotropic cases died in Kern County and 3 out of 35 (8.5 per cent) in Fresno County. The latter included one case of poliomyelitis. Unfortunately not all of the fatalities had confirmatory laboratory findings, so that while they were reported as encephalitis, the actual type frequently remained undetermined. However, one may not always recover a virus from postmortem material, especially if it is sent from a distance. The western equine strain was isolated but 4 times from a total of 34 brains received since 1937. Four of the latter proved to be poliomyelitis, 3 were due to the tubercle organism, one to *Torula histolytica*, one to rabies, and one to *Staphylococcus aureus*. Two of the remaining cases were diagnosed as bulbar poliomyelitis but the others were probably due to encephalitis most likely of the equine type.

AGE AND SEX DISTRIBUTION

Tables 3 and 4 show the age and sex distribution of the cases having antibodies against the equine and the St. Louis viruses for the years, 1939, 1940, and 1941. It is significant that more males than females are affected. This holds true for each year and for both types of viruses. Over twice as many males as females, or 176:82, showed antibodies for the 2 encephalitic strains.

When the data for the 3 years are combined and the ages are subdivided as in Table 4, the male cases still predominate for both viruses. The differences in sex are less noticeable among the younger children through the 12th year, when apparently the chances of exposure to an insect vector are more evenly distributed. On the other hand, owing to the more exposed outdoor life of the men in these agricultural regions, males over 13 years of age seemed to run a greater risk of becoming infected than females. This is also true for the

TABLE 3

Age and Sex Incidence for Encephalitic Cases in Valley Areas

Year	Positive to Virus	Total Number	Sex		Total Number Cases Tested	Age Incidence According to Positive Neutralization Tests			
			Male	Female		Under 1 Year	1–9 Years	10–19 Years	20 Years and Over
1939	W. equine	83	51 (61.4%)	18 (21.6%)	82	8 (9.7%)	23 (28.0%)	20 (24.3%)	17 (20.7%)
	St. Louis alone		9 (10.8%)	5 (6.0%)		1 (1.2%)	2 (2.4%)	6 (6.0%)	5 (6.0%)
	W. equine and St. Louis		16 (19.2%)	2 (2.4%)		1 (1.2%)	5 (6.0%)	4 (4.8%)	4 (4.8%)
1940	W. equine	105	61 (58.0%)	29 (27.6%)	102	19 (18.6%)	24 (23.5%)	14 (13.7%)	30 (29.4%)
	St. Louis alone		9 (8.5%)	6 (5.7%)			2 (1.9%)	6 (5.8%)	7 (6.8%)
	W. equine and St. Louis		15 (14.2%)	8 (7.6%)		3 (2.9%)	5 (4.9%)	7 (6.8%)	8 (7.8%)
1941	W. equine	70	28 (40%)	19 (27.1%)	69	7 (10.1%)	10 (11.5%)	12 (17.3%)	14 (20.2%)
	St. Louis alone		20 (28.5%)	5 (7.1%)			7 (10.2%)	9 (13.0%)	10 (11.5%)
	W. equine and St. Louis		14 (20.0%)	9 (12.8%)		1 (1.4%)	2 (2.9%)	9 (13.0%)	6 (8.7%)

similar age periods in regard to exposure to the St. Louis virus.

All ages are affected by the western equine virus, varying from 16 days to 74 years, with the largest proportion in the group 0–10 years. There are also many cases among males 10 to 30 years old. In Kern County alone, for 1938, 1939, and 1940 [6] the largest number of equine encephalomyelitic cases were under 10 years of age with many among infants under 1 year.

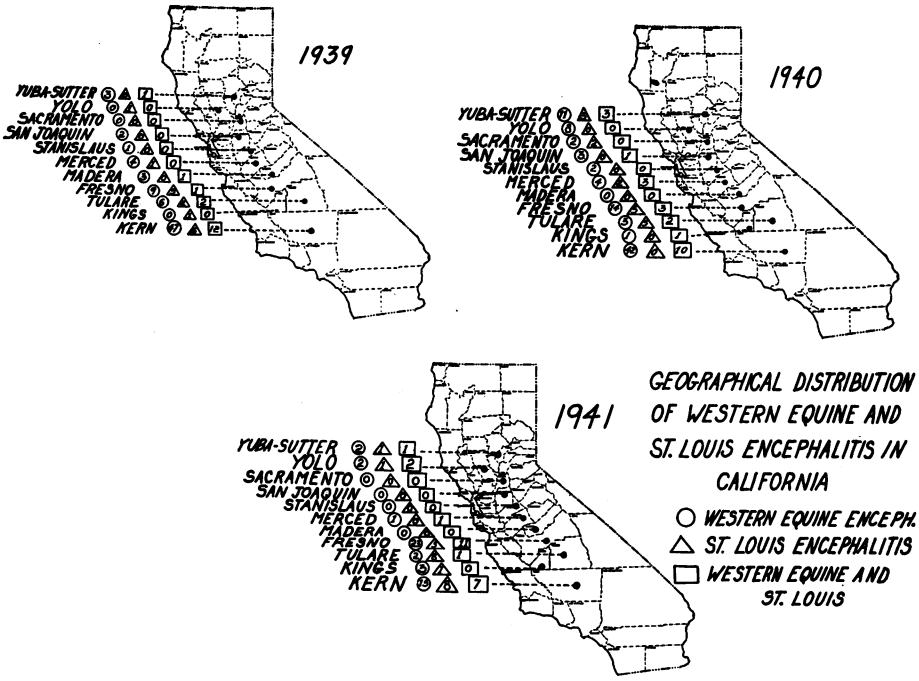
In California the ages most affected by St. Louis virus seem to lie between 13 and 30, with few cases among the younger groups, the range in age extending from under 1 to 66 years. One 6 months old baby had antibodies only for the St. Louis strain. A month old child, 5 infants of 2 months, and another infant of 3 months were positive for both the St. Louis and the equine viruses. The serum of a 20 day old baby with encephalitis showed weak neutralizing ability when first tested for the St. Louis strain but was negative 2 weeks later. The mother had strong antibodies against this virus and it seems probable that the child had acquired them through placental trans-

TABLE 4

Encephalitic Cases in the Central Valleys by Age and by Sex. Neutralization Tests Positive for the Virus for 1939, 1940, 1941

Age Groups	Western Equine			St. Louis Alone			Western Equine and St. Louis		
	Male	Female	Total	Male	Female	Total	Male	Female	Total
0–1	24	16	40	2	0	2	5	2	7
2–6	18	18	36	2	4	6	3	4	7
7–12	18	16	34	3	3	6	6	6	12
13–19	26	6	32	10	6	16	11	4	15
20–29	20	4	24	10	2	12	7	2	9
30–39	14	1	15	3	1	4	3	0	3
40–49	5	2	7	4	0	4	3	1	4
50–59	9	2	11	2	0	2	5	1	6
60–69	3	2	5	1	0	1	0	1	1
73–74	1	1	2	0	0	0	0	1	1
Total	138	68	206	37	16	53	43	22	65

MAP 1—Geographical Distribution of Western Equine and St. Louis Encephalitis in California for 1939, 1940, and 1941 as Determined by the Serum Neutralization Tests



fer. Antibodies for the equine virus predominated in the child's serum but were absent in that of the mother.

The individuals showing a combined antibody response were mainly from 7 to 30 years of age. More of these were positive among the younger groups than were those reacting to the St. Louis strain alone.

GEOGRAPHICAL DISTRIBUTION

It has been previously demonstrated [2,6] that human equine encephalomyelitis occurs in certain definite localities of California. It not only reappears in the same counties but in the same towns or rural districts. Quite often these regions are associated with swampy low lands near irrigation canals or pools of stagnant water. Since the two central valleys have rivers draining from the high Sierra Mountains on the east and from the Coast Range on the west, the water tends to concentrate in the center of the wide valleys over extensive areas. This portion is also the center of population and of agricultural industries. The distribution of the disease for the years 1939, 1940, and 1941 may be followed by reference to Map 1. It must be taken into consideration, however, if the large cities are designated, that the patients resided mainly in the outlying districts. The majority have originated from rural areas, small farms or homes of about an acre on which chickens and other domestic fowl, cows or other animals may be present. Though the affected place may be free of such animals, they are often found somewhere in the neighborhood. Everywhere in the endemic areas, mosquitoes are present some time during the spring or summer.

It is of interest that the individuals showing antibodies to the St. Louis virus often reside in the same regions

where the equine disease is prevalent both among man and horses. A glance at the map shows that the similarity of distribution is striking.

SEASONAL INCIDENCE

Each year there is a definite seasonal occurrence for both of the encephalitic diseases. The first human cases may appear about May or June in the southerly counties of the San Joaquin Valley and later in those further north. They are prevalent during the hot summer months and often continue into the fall or even winter if the weather remains warm. This condition is especially noticed in Kern and Fresno Counties.

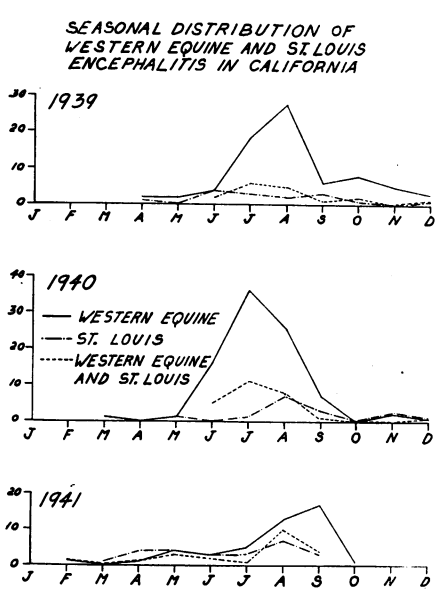


CHART 2—Seasonal Incidence of Western Equine and St. Louis Encephalitis in the Central Valleys of California for 1939, 1940, and 1941

The highest incidence of the equine type throughout the two central valleys, as estimated by the number of serum neutralization tests was in August for 1939, in July for 1940, and in September for 1941 (see data in Chart 2). The cases with antibodies only for the St. Louis virus exhibited the same seasonal appearance with a slightly higher incidence in August. When antibodies were demonstrated for both types of viruses, the cases usually followed the distribution given for the equine form.

In order to correlate the seasonal appearance of encephalomyelitis in the human population with that among the horses, the official reports to the State Department of Agriculture have been used through the courtesy of Dr. C. U. Duckworth. It was noticed that if the data for the valley counties as a whole were compared, the frequency of the equine disease paralleled that of the human, but if they were considered by separate counties, the greatest incidence for the horses occurred approximately one month prior to that for man. This regional difference is in all probability conditioned by the late appearance of an insect vector in the more northerly sections of the state.

It should be emphasized that the cases in horses which come to the attention of the veterinarians, have been diagnosed almost entirely by the clinical symptoms unconfirmed by laboratory findings, while the majority of human encephalitides have been differentiated by the serum neutralization test. Nevertheless, in the counties with the highest incidence, sick horses and human cases of encephalitis are often in close, but not necessarily intimate association. Affected individuals may not possess a horse, yet sick animals might be within one-half to one mile distance.

Not only is the seasonal incidence coincidental for the two encephalitic diseases but poliomyelitis also occurs simultaneously in the same areas. In Kern, Tulare, and Fresno Counties the incidence of poliomyelitis may fluctuate each year but nevertheless sporadic cases are always to be found. Both these diseases are definitely endemic.

PRESENCE OF NEUTRALIZING ANTIBODIES IN HORSE AND FOWL SERA

The simultaneous presence of neutralizing substances for both the St. Louis and the western equine viruses in many human sera and the demonstration of antibodies against the latter strain in the sera of domestic fowl [9] prompted the further examination of blood samples of animals from different regions. Since a preliminary report has already been made,[10] only a brief statement is deemed necessary. It was found that antibodies against the St. Louis and the western equine viruses could be demonstrated in a certain percentage of both horse sera and those of domestic fowl; chickens, turkeys, ducks, pigeons, pheasants, and peacocks, and that more positive results were obtained from endemic than from non-endemic areas. The sera of 32 chicks hatched in the laboratory were all negative. Comparatively few sera showed antibodies only for the St. Louis virus. However, the percentage was high, 77.7 per cent of 46 animals, when the sera yielded reactions for both types.

With the exception of a few horses, most of the animals tested were apparently normal. It has been demonstrated by Ten Broeck [11] and by Howitt [9] that domestic fowl may remain clinically unaffected by the equine virus and yet carry the latter in the peripheral circulation for a certain period of time. Further experiments have shown that young chicks may remain well after inoculation with the St. Louis strain and yet harbor virus in the blood through the 30th hour. The possibility of these inapparent infections in relatively insusceptible animals, especially fowl, strongly suggests the barnyard as a potential reservoir for the encephalitic viruses, particularly since both types have recently been recovered from the mosquito, *Culex tarsalis,* by Hammon, Reeves, Brookman, Izumi, and Gjullin.[12] Hammon and associates have also [13] reported the results of testing the sera of a large group of birds and mammals in the Yakima Valley and found a higher percentage neutralizing the equine or the St. Louis viruses among domestic than wild animals.

NEUTRALIZATION TESTS ON SERA OF NON-ENCEPHALITIC INDIVIDUALS

It has always been a question as to what interpretation to place on the results of the neutralization tests for the encephalitic cases. Does a positive test indicate contact with the disease and how many members of the population might be expected to have neutralizing antibodies? Buss and Howitt [6] have reported the tests against the western equine virus made on sera of normal individuals in the endemic areas of Kern County. Of 82 friends and relatives of acute cases, the sera of only 6 (7.3 per cent) were positive, while 97 (86.6 per cent) of 112 sera from acute encephalitic patients in the same areas reacted to the equine virus. Of 82 bloods from cases of poliomyelitis, only 5 (6.0 per cent) neutralized this strain. Thus a normal expectancy of 6.6 per cent positive neutralization tests for the equine virus is probably correct for a comparable group of non-encephalitic individuals in an endemic region. When one takes into account the findings on sera tested from a non-endemic district like the San Francisco Bay region together with the low figures for the normal group in an endemic area, the higher percentages for the acute cases acquire definite significance and the test would appear of value as a diagnostic aid for the equine disease.

The results, however, are not as conclusive in regard to the value of the neutralizing antibodies against the St. Louis virus, since many human beings in the general population may be

affected in an endemic region. In a series of 144 sera received from people in the Bay Area during the past 3 years, only one (0.6 per cent) has given a weakly positive reaction. In another group of sera from poliomyelitic cases in the coastal city of Tacoma, Wash., only 4 (6.4 per cent) were positive to the St. Louis virus as compared to 28 per cent or 7 times the number reported by Hammon [14] and by Hammon and Howitt [15] for a group among non-encephalitic people in the endemic Yakima Valley, Wash.

Blood from a comparable group of either poliomyelitic patients or normal contacts has been tested from the valley regions of California. Of 95 sera, 15 (15.7 per cent) were positive for the St. Louis virus or an expectancy of over twice as many for this disease among the normal population in the same areas as for the equine strain. The percentage of positive tests in this endemic region was about one-half that among the normal individuals as for those in the Yakima Valley, where a higher incidence is found for the St. Louis virus.[14,15] From the data collected it would seem that the presence of antibodies for the St. Louis strain may not be as etiologically significant in the diagnosis as their presence for the western equine virus in a similar area.

Notwithstanding, it appears that the St. Louis virus is the responsible agent for a number of the acute encephalitic cases in certain districts and that the presence of protective substances in the blood would be of diagnostic importance among the younger age groups. Positive tests for this strain alone were obtained on the sera of 2 encephalitic infants under 1 year and on those of 7 when in combination with antibodies for the equine virus. Six children under 6 years of age were also positive only to the St. Louis virus. The ages responsible for most of the positive tests, however, remain in the older groups, mainly 12 to 30 years.

In most localities the western equine virus is apparently the more predominant agent of the 2 diseases as shown by the greater number of positive protection tests among the acute cases, although the St. Louis type has been more in evidence in Tulare County during 1940 and 1941. A total of 140 tests were positive for only the equine strain as compared to 55 for only the St. Louis during the past 3 years, or over 2½ times as many for the equine virus. Although the St. Louis strain itself has not so far been recovered in California, yet it seems likely that it is present, but not of as great a significance as the western equine virus.

NEUTRALIZATION TESTS ON SERA FROM OTHER CALIFORNIA DISTRICTS

While the major portion of the blood samples have come from the two central valleys of California, yet a small number have also been received from the southern part of the state. No positive tests were obtained against the equine virus until 1941 when the serum of one man from Orange County contained neutralizing antibodies. The patient resided in the town and seldom went elsewhere. Horses, however, have been known to contract encephalitis in the same county, so that the virus is probably to be found.

It seems probable that the St. Louis virus may likewise be responsible for human cases in these districts, since in 1938 encephalitis was reported in Riverside. At that time 6 (46.1 per cent) of 13 sera were positive for the St. Louis virus and none for the equine. The serum of one was weakly positive at first and became stronger after recovery. Seven sera did not react to either strain, although 3 of them were tested again several months after the onset. It seems likely that the St. Louis virus was responsible for this

small outbreak even though no active agent was recovered.

Because the eastern virus of equine encephalomyelitis has recently been reported in horses as far west as Texas,[16] there might be a possibility of such an occurrence along the Pacific slope. Sera have been received from many encephalitic patients in the coastal counties but all have been negative to the western virus. Likewise certain individuals in the central valleys have been clinically typical of encephalitis but without antibodies to the viruses used even after repeated tests. For this reason 11 sera from Kern County and an equal number from the Bay region and neighboring counties were tested against the eastern equine virus. Ten cases positive to the western strain from the valleys were also included. All sera so far have been negative except from one patient in Alameda County. He had been given large amounts of drugs and antimeningococcus serum as well, so that there is a possibility of an inhibitory action on the virus. Unfortunately no more serum was obtained to determine whether the blood became negative later.

DISCUSSION

From the clinical histories and from the results of many neutralization tests made each year, it seems evident that the virus of western equine encephalomyelitis has become endemic for man in California, probably for a longer period of time than can be estimated. Undoubtedly many cases have passed as non-paralytic poliomyelitis. Although the disease has never reached the epidemic proportions reported by Leake [17] in 1941 for North Dakota and the northern midwestern states, yet the constant recurrence each year in the same localities renders a burden on the community and leads to a condition of disquiet in the rural population during the summer season. It is true that many cases recover without residual effects, but on the other hand all stages of the disease may be seen, hence the physicians are becoming cognizant that permanent defects to the nervous system may be expected. The neutralization test has been of value in the diagnosis of these cases that now are referred to the urban physician from rural communities for consultation. Often they appear many months after the acute attack, with eye defects, personality changes or a state of mental retardation bordering on imbecility. These residuals have been less frequent among adults, although eye troubles and headaches may persist for some time.

The history of a particular case illustrates the sequel. A 5 year old boy was taken ill in 1937. He had convulsions, was weak, emaciated, and was expected to die at any time, but recovered. His blood gave a positive neutralization test for western equine virus and was checked again in 1938. The boy improved physically but lacked coördination and spoke incoherently. In 1941, 4 years after the onset of the disease, he had grown strong but was mentally defective and still lacking in coördination.

Since it is now known [12] that the mosquito, *Culex tarsalis,* is capable of carrying the western equine and also the St. Louis virus, every precaution should be taken against mosquito bites in endemic areas; children especially should be protected. The attack rate of infants and young children under 12 years has been high in the valley regions, contrary to the findings of Leake [17] in North Dakota, where the adults were mainly affected.

In 1937, when cases of encephalitis first became of importance in the state, the evidence seemed to indicate the virus of St. Louis encephalitis as the active agent. Over 50 per cent of the encephalitic patients had neutralizing

antibodies for this strain in their blood but no virus was found.[18] After recovery of the western equine strain from man in 1938 and when the serum neutralization tests indicated the widespread incidence in these regions, the latter disease took precedence and the significance of the St. Louis encephalitis was correspondingly minimized. A combination of circumstances at the time of first reporting suggested that the antibodies for the St. Louis virus, especially if together with those for the equine, had been acquired previously. Many of the sera were from people in the older age group who could have had an earlier infection. Many individuals were migratory laborers and it was suggested that they had brought in the disease to the state or had acquired it through contact with their neighbors.

From experimental evidence and data collected since that period, it seems that the previous impression of introduction by the migrants, largely prompted by testing only human sera, should now be corrected. The finding of antibodies for the St. Louis virus in sera of horses, domestic fowl, and wild mammals, together with their presence in the blood of infants under 1 year, furnishes convincing evidence that this virus has been endemic in the state for some time, although it has not as yet been recovered from human or animal tissues. While there was no very marked difference in percentage between the number of tests positive for the St. Louis virus from normal people (15.7 per cent) and those with encephalitis (27.7 per cent), yet undoubtedly clinical cases are present.

It is probable that one is dealing with two types of encephalitis in the same community, due to two different viruses. Experimentally the strains are immunologically and serologically distinct, but by producing a mixed infection in monkeys it has been shown[19] that a highly virulent western equine virus may take precedence, inducing the symptoms and the lethal effect. The equine strain is recovered postmortem even though the St. Louis virus may be found in the blood during the first 48 hours after inoculation. Antibodies may be only weakly positive for the latter while those for the equine are promptly evident. It is possible therefore to have neutralizing substances in the blood due to a simultaneous infection with the two separate viruses. That this dual infection may explain the presence of both the equine and the St. Louis antibodies in the same human serum, has been proposed recently in regard to the outbreak of encephalitis in the Yakima Valley.[14,15] The possibility of the dual infection has been given further credence after recovery of both types of viruses from the mosquito as previously mentioned.

Mosquitoes have long been in association with both human and equine cases of encephalitis in California and since the disease is prevalent during the periods of greatest mosquito infestation and in irrigated, cultivated areas conducive to their propagation, it seems probable the same vectors are likewise the responsible agents for the encephalitides in this state.

SUMMARY

The study of encephalitis in California, based largely on the serum neutralization tests, may be summarized for the 3 years 1939, 1940, and 1941:

Of 498 human sera from cases of neurotropic virus disease in the central valleys including poliomyelitis, 213 (42.3 per cent) neutralized the virus of western equine encephalomyelitis, 55 (11.5 per cent) of 475 sera only the St. Louis strain, and 62 (13 per cent) both viruses. If the total amounts for the 3 years are considered, it is shown that 140 tests are positive only to the

western equine virus, exclusive of those in combination with the St. Louis strain, as compared to 55 for the latter virus alone or over 2½ times as many for the equine.

One hundred and forty-four sera from the San Francisco Bay region were negative to the western equine strain with only one (2 per cent) weakly positive to the St. Louis type, although 3 sera from other coastal counties reacted to the latter strain alone.

The western equine virus was recovered from 3 human brains and that of poliomyelitis from 3 others during the 3 year period.

There were over twice as many males as females among the total number of encephalitic cases, although when the ages were subdivided, no sex distinction was noticeable in the youngest age groups infected with the equine virus. All ages were affected by both types but the majority of cases were under 10 years for the equine, and in the years 13 to 30 for the St. Louis strain.

Cases of both the western equine and the St. Louis encephalitis were found mainly in the rural agricultural, irrigated sections throughout the two large Central Californian valleys with a definite seasonal occurrence for both diseases that rises to a peak in July or August or even into September.

A normal expectancy of 6.6 per cent positive neutralization tests for the western equine virus was found among the normal population in an endemic area as compared to 15.7 per cent for the St. Louis strain in the same environment. Consequently more reliance may be placed in the test as a diagnostic aid for the equine disease than for the other.

The sera of 32 encephalitic cases were negative to the eastern equine virus of encephalomyelitis.

Of a small group of sera tested from Southern California during the 3 years only one showed antibodies against the western equine strain, although this virus has been isolated from horses in similar localities. Six cases of encephalitis from one county, however, had neutralizing antibodies against the St. Louis virus.

Occasional residual effects to the central nervous system may be expected after infection with the virus of western equine encephalomyelitis, especially among the children.

From the epidemiological, clinical, and laboratory evidence one may conclude that the virus of western equine encephalomyelitis has become endemic in the central valleys of California for man and animals and that the St. Louis strain is likewise closely associated. From the finding of antibodies in the sera of fowl and mammals in endemic areas and in children under 1 year of age, it is apparent that the St. Louis virus has been in California for some time and is not imported from the mid-western states as formerly proposed.

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