Evaluation of the Epidemic Potential of Western Equine Encephalitis Virus in the Northeastern United States1,2

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The problem of evaluating the epidemic potential of western equine encephalitis in the northeastern United States is presented and possible reasons are discussed for the present lack of human and horse cases of this disease even though increased numbers of isolations of the virus have been obtained in the East during recent years. Epidemiologic factors of vector bionomics and virus strain variations are considered. It is concluded that while this virus strain can no longer be regarded as uncommon in the Northeast, the evidence indicates there is little potential for epidemic expression of this agent in the human and horse population. This appears to be due to differences in the bionomics of the mosquito Culiseta melanura, which serves as the primary enzootic vector in the northeastern United States and in the bionomics of Culex tarsalis that is the vector in the western region of the United States. Other limiting factors in the epidemic potential may be variations between virus strains located in the East and West.

Western equine encephalitis (WEE) virus is classified as an arthropod-borne virus (arbovirus) in the family Togaviridae. It is maintained in nature in a wild bird–mosquito transmission cycle and is one of the most common arboviruses causing encephalitis in man in North America. For over 30 years it has been known to occur in epidemics involving human fatalities in the central and western United States. As an example, an outbreak involving over 3000 cases occurred in North Dakota, Minnesota, and adjacent areas of Canada during the summer of 1941. In this epidemic the case fatality rate ranged from 8 to 15% (1). In addition to the occurrence of sporadic epidemics, the infection of humans and equines, often subclinical, can be detected annually in a number of areas in the central and western United States (2, 3).

Until recent years, WEE virus has been found only infrequently in the Northeast. The initial isolation in this region was made in New Jersey in 1953 (4). Subsequently, virus was recovered in Massachusetts in 1959 (5) and in Maryland in 1964 (6), and it was reported from Connecticut and New York in 1972 and 1973, respectively (7, 8). However, over the past several years, the number of isolations obtained from mosquitoes in this area has increased greatly. Even though WEE virus is present in this region, no illness attributable to infection with this agent has been recognized in humans or equines. The reason for the apparent absence of disease in these hosts in the Northeast is unknown, and the presence of WEE virus is cause for concern that epi-
demic potential exists especially in view of the increasing population density and suburbanization in this region.

VARIATION IN VECTOR BIONOMICS

The geographical variation in disease pattern expressed by WEE virus is probably a reflection of parallel variations that exist in the biology of the virus between the Northeast and the other regions where infection of human and equines is known to occur. In the epidemiology of any arbovirus, three factors are necessary before disease can occur in a locale: (i) the virus; (ii) susceptible vertebrate hosts that become ill when infected with the virus; and (iii) suitable vectors for virus transmission. Numerous isolations from mosquitoes and wild birds establish that WEE is present in the Northeast (9–16). In addition, there is no reason to suspect that humans and equines in this region are any less susceptible than they are in other areas where disease occurs in these hosts. However, an obvious factor that does vary in the biology of WEE virus between these geographical regions is the species of mosquito incriminated as the primary vector responsible for enzootic maintenance. *Culex tarsalis* serves as the vector in the central and western United States while *Culiseta melanura* fills this role in the Northeast (17).

One factor determining the public health threat posed by an arbovirus is the frequency of man’s exposure to infected vectors. In turn, the frequency of exposure of man to mosquito-borne viruses depends on the bionomics of the mosquitoes involved in the transmission cycle. *Cx. tarsalis* and *Cs. melanura* vary considerably in their bionomics.

*Cx. tarsalis* prefers to breed in sunlit grassy marshes, open ground pools containing emergent vegetation, and pools in stream beds. It is particularly abundant in irrigated areas where seepage and improper flooding of pasture lands results in extensive sites favorable to the production of mosquitoes. The irrigated areas of the Great Plains and western North America are the places where WEE virus has been recognized as a disease threat to humans and equines (18). *Cs. melanura* has a more restricted breeding preference and appears to be limited almost entirely to freshwater wooded swamps (15, 19–21). This mosquito often may be the most abundant species within the swamp habitat, and it is seldom collected in any numbers away from such areas. This type of habitat is also where foci of WEE virus activity have been found to occur in the Northeast (17).

In addition, these two species vary in their feeding habits. Although predominantly a bird feeder, *Cx. tarsalis* is opportunistic in its choice of hosts. Precipitin testing of blood-fed specimens has shown that it will readily feed on mammals including horses and man (22, 23). On the other hand, *Cs. melanura* feeds almost exclusively on avian hosts, especially birds in the order Passeriformes (21, 24–30). There have been only three reported observations of this mosquito feeding on man in nature (31–33). Blood-meal identification by precipitin testing has revealed only a few additional cases (6, 25). Reports of *Cs. melanura* feeding on equines have been even less frequent: Chamberlain and co-workers collected three specimens feeding on a mule in North Carolina (34). In addition, precipitin testing of females collected in Maryland resulted in the finding of only two specimens positive for horse blood (6, 12).

These behavioral differences between *Cx. tarsalis* and *Cs. melanura* indicate that the absence of WEE in humans and equines in the Northeast may be due in part to a lack of exposure to infected vectors. In other words, *Cs. melanura* is not coming out of the swamp habitat to feed on these hosts, and, if the hosts occasionally wander into
areas occupied by this vector during the hours of darkness when it would normally be feeding, its host preferences are such that it is still unlikely to feed on them.

Results from limited serological surveys support the conclusion that humans and equines are not exposed to WEE virus in the Northeast (17). However, before this hypothesis can be accepted, the occurrence of cases of eastern equine encephalitis (EEE) in these hosts has to be considered, since results from both field and laboratory studies have implicated *C. melanura* as the primary enzootic vector of this disease as well (35, 36). Like WEE, the virus of EEE is also a member of the Togaviridae and is maintained in nature in a wild bird-mosquito cycle. Enzootic foci of this virus also have generally been found to be limited to the wooded freshwater swamp habitat; however, in addition, a number of cases of EEE in humans has been reported in this area (2). Equine deaths also are reported annually from EEE, and several large epizootics have been attributed to infection with this virus (17).

There is no evidence from virus isolation from mosquitoes and wild birds or from antibody prevalence rates in wild birds to indicate that *C. melanura* is a less efficient vector for WEE virus than for EEE virus or that the virus of WEE is less prevalent in this region than the virus of EEE. In addition, WEE virus, at least occasionally, escapes from the freshwater swamp since the virus has been isolated from penned pheasants and wild birds such as the house sparrow which are rarely found in this type of habitat (17).

A possible explanation for the different disease picture presented by the viruses of EEE and WEE in the Northeast is that other mosquito species besides *C. melanura* serve as epidemic vectors and carry EEE, but not WEE, out of the swamp to humans and horses. Several *Aedes* species have been implicated as possible vectors of EEE virus. Because of their abundance, feeding habits, and distribution, *Aedes sollicitans* and *A. vexans* have the highest index of suspicion in the Northeast (13, 37, 38).

A number of isolations of EEE has been reported from these two species in this region (39). Also, studies in the laboratory have shown that both *A. sollicitans* and *A. vexans* are capable of vectoring the virus of EEE experimentally, and, in one instance, *A. sollicitans* was shown capable of transmitting EEE virus from an infected to a susceptible horse (41–43). In addition, WEE virus has been isolated from *A. vexans* in the Northeast, but no isolations have been made from *A. sollicitans* in this area, although both of these species have also been shown capable of transmitting WEE virus experimentally (41, 44).

If these two species or other vectors are serving to bring EEE virus out of the enzootic habitat to man and equines, and if these species are less susceptible to infection with the virus of WEE than to infection with the virus of EEE, this could account for the apparent differences in “escape” rate presented by these two viruses in the Northeast. This explanation would also be compatible with the previous hypothesis that the differences in the bionomics of *C. melanura* and *Cx. tarsalis* explain the different occurrence of illness caused by WEE virus in the eastern and western geographical areas of the United States.

**VIRUS STRAIN VARIATION**

Variation in the strains of WEE virus between geographical regions may play a role in the disease pattern presented by this agent in different areas. For example, even though WEE virus is present in the Northeast, strains which occur in this area may be less virulent for humans and equines than strains present in the central and western United States. Karabatsos and co-workers were able to show that strains of
WEE virus isolated from different geographical areas were distinct antigenically (45). Four strains of virus isolated in the western United States and Canada were indistinguishable from each other but differed from three strains isolated in the East. In a continuation of these studies, Henderson compared 100 strains of WEE virus isolated from different geographical regions (46). He was able to separate these strains into three distinct groups based on antigenic properties. All of the viruses originating from along the Atlantic and Gulf Coast regions formed a homogeneous group while the viruses isolated in the central and western parts of the country formed two antigenic groups which overlapped in their range of distribution. The single exception to the above pattern was a virus strain from Colorado which was antigenically similar to the strains from the eastern United States.

In addition, Henderson et al. reported that passage of virus strains through certain vertebrate host systems resulted in alteration of antigenic properties. These results led to the hypothesis that each strain of WEE virus apparently was composed of a number of subpopulations of virions with distinct properties and that differences between strains were due to qualitative and quantitative differences in the subpopulations comprising the strains (47, 48).

Several other arboviruses that are transmitted by mosquitoes have been shown to have antigenic variation relating to geography (49–52). Such geographic patterns of antigenic variation led to the formation of a hypothesis by Shope (53,) as follows.

Perhaps arthropod-borne virus strains vary from place to place because in different geographical locations they encounter different host species and different vector species which determine the antigenic population making up the predominant serological type in a given locality. This hypothesis would also explain the antigenic stability over the years in a given location... where the vertebrate and mosquito populations are relatively stable.

Such a mechanism of selection and stabilization may be applicable to the strain variation encountered with WEE virus. Although the same wild birds that are common to many areas appear to be involved as vertebrate hosts in the ecology of this virus, as mentioned earlier, the primary mosquito host systems are distinct in the eastern and in the western United States. Circulation of WEE virus in these different vector systems over a period of time may have resulted in the selection of different subpopulations of virions resulting in the geographic pattern of antigenic variation between virus strains now recognized.

In attempting to illustrate this experimentally, Henderson et al. (47) used mixtures containing varying proportions of purified strains of WEE virus antigenic types but found no preferential selection of one population over the other after one oral passage through Aedes aegypti. However, experimental studies on the alteration of the antigenic character of distinct virus strains from different geographical regions after serial passage through the reciprocal natural vectors have not been conducted.

In addition to studies on antigenic differences, one study has been reported comparing the virulence for equines of strains of WEE virus from various geographic areas. A strain of WEE virus that was originally isolated from Cs. melanura collected in Florida was compared to three strains from western North America (54). The strain from Florida was less virulent than the other three viruses. It caused no detectable illness in ponies inoculated intracerebrally. All of the ponies inoculated with the strains of WEE virus from western North America developed an elevated body temperature and five of six developed clinical signs of encephalitis. However, strains of WEE virus from the Northeast have not been tested experimentally for virulence to equines.

Even if strains of virus from the Northeast are less virulent, the possibility of WEE
virus producing illness in humans and equines at some time in the future may still exist if more virulent strains of virus from the central and western United States were introduced into this area and became established. The opportunity for such an introduction appears to exist in view of the extensive overlap in the distribution of *Cx. melanura* and *Cx. tarsalis* (55–59). Although *Cs. melanura* has not been reported in the far West, it does occur in the central part of the country as well as in the eastern United States. In the East, *Cx. tarsalis* occurs in most of the southern states but has been reported only as far north as Pennsylvania.

Such a situation would be analogous to a recent epidemic in Texas caused by another virus in the family Togaviridae, Venezuelan equine encephalitis (VEE). This outbreak was apparently caused by an “epidemic” strain of VEE virus introduced into the Pacific Coast of Central America from Ecuador in 1969 and eventually spread into the southern United States during the summer of 1971. Endemic strains of VEE virus had apparently existed for over 50 years without causing a serious outbreak of human disease in the area of Central America where the epidemic started (60).

**CONCLUSIONS**

WEE virus can no longer be considered uncommon in the northeastern United States because of numerous isolations from mosquitoes, especially *Cs. melanura*, and from wild birds. However, the available evidence indicates that there is little potential for epidemic expression of this agent in the human and equine population. This appears to be in part due to differences between the bionomics of *Cs. melanura* which serves as the primary vector in the northeastern United States and the bionomics of *Cx. tarsalis* which serves as the vector in other areas of the country where the virus is responsible for disease in these hosts. In addition, variation of WEE virus strains from geographic locations in the East and in the West occurs, and, if this variation includes reduced mammalian pathogenicity of the eastern strains as compared to the western strains, this may also be a limiting factor in the epidemic potential of WEE in this region.

**REFERENCES**

1. Olitsky, P. K., and Casals, J., *In “Viral Encephalitides. Viral and Rickettsial Infections of Man.”* (M. Rivers, Ed.), 2nd ed., Chap. 11, pp. 214–266. J. B. Lippincott, Philadelphia, 1952.
2. McGowan, J. E., Jr., Bryan, J. A., and Gregg, M. B., Surveillance of arboviral encephalitis in the United States, 1955–1971. *Amer. J. Epidemiol.* 97, 199–207, 1973.
3. Reeves, W. C., and Hammon, W. McD., Epidemiology of the arthropod-borne viral encephalitides in Kern County, California, 1943–1952. *Univ. Calif. Publ. Public Health* 4, 257 pp. University of California Press, Berkeley, Calif., 1962.
4. Holden, P., Recovery of western equine encephalomyelitis virus from naturally infected English sparrows of New Jersey, 1953. *Proc. Soc. Exp. Biol. Med.* 88, 490–492, 1955.
5. Hayes, R. O., Daniels, J. B., and MacCready, R. A., Western encephalitis virus in Massachusetts. *Proc. Soc. Exp. Biol. Med.* 108, 805–808, 1961.
6. Moussa, M. A., Gould, D. J., Nolan, M. P., Jr., and Hayes, D. E., Observation on Culiseta melanura (Coquillett) in relation to encephalitis in southern Maryland. *Mosq. News* 26, 385–393, 1966.
7. Yale Arbovirus Research Unit, unpublished observations.
8. Woodall, J. P., personal communication.
9. Chamberlain, R. W., Sudia, W. D., Burbulis, P. P., and Bogue, M. D., Recent isolations of arthropod-borne viruses from mosquitoes in eastern United States. *Mosq. News* 18, 305–308.
10. Kandle, R. P., Summary of our present knowledge of EE in New Jersey. *Proc. Annu. Meeting N.J. Mosq. Exterm. Ass.* 48, 15–20, 1961.
11. Kandle, R. P., A look at arbovirus research activities in New Jersey. *Proc. Annu. Meeting N.J. Mosq. Exterm. Ass.* 50, 16–21, 1963.
12. Kandel, R. P., Continued arbovirus research activities in New Jersey. Proc. Annu. Meeting N.J. Mosq. Exterm. Ass. 51, 1-5, 1964.
13. Goldfield, M., and Sussman, O., Eastern encephalitis in New Jersey during 1969. Proc. Annu. Meeting N.J. Mosq. Exterm. Ass. 57, 1970.
14. Dalrymple, J. M., Young, O. P., Eldridge, B. F., Russell, P. K., Ecology of arboviruses in a Maryland freshwater swamp. III. Vertebrate hosts. Amer. J. Epidemiol. 92, 129-140, 1972.
15. Saugstad, E. S., Dalrymple, J. M., and Eldridge, B. F., Ecology of arboviruses in a Maryland freshwater swamp. I. Population dynamics and habitat distribution of potential mosquito vectors. Amer. J. Epidemiol. 96, 114-122, 1972.
16. Encephalitis Field Station, Massachusetts Department of Public Health, unpublished data.
17. Hayes, C. G., and Wallis, R. C., Ecology of western equine encephalitis in the eastern United States. Advan. Virus Res., in press, 1976.
18. Hess, A. D., Harmston, F. C., and Hayes, R. O. Mosquito and arbovirus disease problems of irrigated areas in North America. In “CRC Critical Reviews in Environmental Control,” pp. 443-465. CRC, Cleveland, Ohio, 1970.
19. Jambback, H., Culiseta melanura (Coquillett) in New Jersey. Proc. Annu. Meeting N.J. Mosq. Exterm. Ass. 43, 1956.
20. Jambback, H., Culiseta melanura (Coq.) breeding on Long Island. N. Y. Mosq. News. 21, 140-141, 1961.
21. Joseph, S. R., and Bickley, W. E. Culiseta melanura (Coquillett) on the Eastern Shore of Maryland (Diptera: Culicidae). Univ. Maryland Agr. Exp. Sta. Bull. A-161, 1969.
22. Tempelis, C. H., Reeves, W. C., Bellamy, R. C., and Lofty, M. F., A three-year study of the feeding habits of Culex tarsalis in Kern County, California. Amer. J. Trop. Med. Hyg. 14, 170-177, 1965.
23. Tempelis, C. H., and Washino, R. K., Host-feeding patterns of Culex tarsalis in the Sacramento Valley, California, with notes on other species. J. Med. Entomol. 4, 315-318, 1967.
24. Hayes, R. O., Host preferences of Culiseta melanura and allied mosquitoes. Mosq. News. 21, 179-187, 1961.
25. Jobbins, D. M., Burbutis, P. P., and Crans, W. J., Mosquito blood-meal determinations—A cooperative project. Proc. Annu. Meeting N.J. Mosq. Exterm. Ass. 48, 211-215, 1961.
26. Crans, W. J., Blood meal preference studies with New Jersey mosquitoes. Proc. Annu. Meeting N.J. Mosq. Exterm. Ass. 49, 120-126, 1962.
27. Crans, W. J., Continued host preference studies with New Jersey mosquitoes, 1963. Proc. Annu. Meeting N.J. Mosq. Exterm. Ass. 51, 50-58, 1964.
28. Means, R. G., Host preferences of mosquitoes (Diptera: Culicidae) in Suffolk County, New York. Ann. Entomol. Soc. Amer. 61, 116-120, 1968.
29. Edman, J. D., Webber, L. A., and Kale, H. W., II, Host feeding patterns of Florida mosquitoes. II. Culiseta. J. Med. Entomol. 9, 429-434, 1972.
30. Le Duc, J. W., Suyemoto, W., Eldridge, B. F., and Saugstad, E. S., Ecology of arboviruses in a Maryland and freshwater swamp. II. Blood feeding patterns of potential mosquito vectors. Amer. J. Epidemiol. 96, 123-128, 1972.
31. Stabler, R. M., Notes on certain species of mosquitoes from Delaware County, Pennsylvania. Mosq. News. 8, 17-19, 1948.
32. Hayes, R. O., and Doane, O. W., Jr., Primary record of Culiseta melanura biting man in nature. Mosq. News. 18, 216-217, 1958.
33. Schober, H., Notes on the behavior of Culiseta melanura (Coq.) with three instances of its biting man. Mosq. News. 24, 67, 1964.
34. Chamberlain, R. W., Sudia, W. D., Coleman, P. H., Johnston, J. G., Jr., and Work, T. H., Arbovirus isolations from mosquitoes collected in Waycross, Georgia, 1963, during an outbreak of equine encephalitis. Amer. J. Epidemiol. 89, 82-88, 1969.
35. Howard, J. J., and Wallis, R. C., Infection and Transmission of eastern equine encephalomyelitis virus with colonized Culiseta melanura (Coquillett). Amer. J. Trop. Med. Hyg. 23, 522-525, 1974.
36. Wallis, R. C., and Main, A. J., Eastern equine encephalitis in Connecticut, progress and problems. Mem Conn. Entomol. Soc. 1974 117-144, 1974.
37. Wallis, R. C., Mosquitoes in Connecticut. Conn. Agr. Exp. Sta. Bull. 632, 1960.
38. Feemster, R. F., and Getting, U. A., Distribution of the vectors of equine encephalomyelitis in Massachusetts. Amer. J. Public Health 31, 791-802, 1941.
39. Beadle, L. D., Eastern equine encephalitis virus from mosquitoes collected in 5 northeastern and 5 southeastern states 1948-1972. Unpublished mimeographed sheet, 1973.
40. Davis, W. A., A study of birds and mosquitoes as hosts for the virus of eastern equine encephalomyelitis. Amer. J. Hyg. 32, 45-59, 1940.
41. Chamberlain, R. W., Sikes, R. K., Nelson, D. B., and Sudia, W. D., Quantitative determination of virus-vector relationships. *Amer. J. Hyg.* 60, 278–285, 1954.

42. Sudia, W. D., Stamm, D. D., Chamberlain, R. W., and Kissling, R. E., Transmission of eastern equine encephalitis to horses by *Aedes sollicitans* mosquitoes. *Amer. J. Trop. Med. Hyg.* 5, 802–808, 1956.

43. Kelser, R. A., Transmission of the virus of equine encephalomyelitis by *Aedes taeniorhynchus*. *J. Amer. Vet. Med. Ass.* 92, 195–203, 1938.

44. Goldfield, M., personal communication.

45. Karabatsos, N., Bourke, A. T. C., and Henderson, J. R. Antigenic variation among strains of western equine encephalomyelitis virus. *Amer. J. Trop. Med. Hyg.* 12, 408–412, 1963.

46. Henderson, J. R., Immunologic characterization of western equine encephalomyelitis virus strains. *J. Immunol.* 93, 452–461, 1964.

47. Henderson, J. R., Shah, H. H., and Wallis, R. C., Antigenic variants of arboviruses. I. The host as a determinant in the evolution of strain variants. *Virology* 26, 326–332, 1965.

48. Henderson, J. R., Levine, S. I., Stim, T. B., and Karabatsos, N., Antigenic variants of arboviruses. III. Host passage of constituent antigen subpopulations of strains. *J. Immunol.* 99, 935–944, 1967.

49. Clarke, D. H., Antigenic variation and geographic distribution of arboviruses. *An. Microbiol.* 11, 143–148, 1963.

50. Casals, J., Antigenic variants of eastern equine encephalitis virus. *J. Exp. Med.* 119, 547–565, 1964.

51. Hammon, H. M., Clarke, D. H., and Price, W. H., Antigenic variation of West Nile in relation to geography. *Amer. J. Epidemiol.* 82, 40–55, 1965.

52. Young, N. A., and Johnson, K. M., Antigenic variants of Venezuelan equine encephalitis virus. Their geographic distribution and epidemiologic significance. *Amer. J. Epidemiol.* 89, 286–305, 1969.

53. Shope, R. E., Antigenic variation among arboviruses. *Cienc. Cult.* 17, 30–32, 1965.

54. Sponseller, M. L., and Binn, L. N., Wooding, W. L., and Yager, R. H., Field strains of western encephalitis virus in ponies: Virologic, clinical, and pathological observations. *Amer. J. Vet. Res.* 27, 1591–1598, 1966.

55. Carpenter, S. J., and LaCasse, W. J., “Mosquitoes of North America (North of Mexico),” 360 pp. University of California Press, Berkeley and Los Angeles, Calif., 1955.

56. Carpenter, S. J., Review of recent literature of mosquitoes of North America. *Calif. Vector News* 15, 72–97, 1968.

57. Carpenter, S. J., Review of recent literature of mosquitoes of North America. Supplement I. *Calif. Vector News* 17, 40–65, 1970.

58. Brieb, C. G., Reported in Supplement of 48th Annual Meeting of New Jersey Mosquito Extermination Association, by Helen Sollers-Riedel. 1970. World studies on mosquitoes and diseases carried by them. 1971.

59. Snow, W. E., and Pickard, E., Seasonal history of *Culex tarsalis* and associated species in larval habitats of the Tennessee Valley Region. *Mosq. News* 16, 143–148, 1956.

60. Franck, P. T., Significance of geographic distribution of VEE virus variants. In “Symposium on Venezuelan Encephalitis Virus,” Scientific Publication No. 243, pp. 322–328. Pan American Health Organization, Washington, D.C., 1972.