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# Arthropod-borne encephalitides in the Americas*

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*The arthropod-borne encephalitides are an important cause of equine and human morbidity in the Americas. Between 1975 and 1978, 6970 human cases of arboviral encephalitis were reported in the United States of America; however, this represents only a fraction of the true incidence. St Louis encephalitis (4824 cases), California encephalitis (1035 cases), and western equine encephalitis (WEE, 947 cases) accounted for 98.5% of all reported infections. Approximately 1000–4000 cases of equine encephalitis occur annually in the United States, the majority due to WEE. In tropical America, important outbreaks of Venezuelan, eastern, and western equine encephalitis, and of Rocio encephalitis have occurred.*

*In this article, epidemiological aspects of arboviral encephalitis outbreaks occurring within the past 5 years are reviewed. In addition, summaries of current research activities on the ecology and epidemiology of St Louis, western equine, Venezuelan equine, Rocio, and California encephalitis viruses are presented, and the problem of control of these infections is discussed.*

The arthropod-borne viral encephalitides are an important cause of human and equine morbidity in the Americas. Nearly all the cases involve one of seven viruses, six of which are transmitted by mosquitos (St Louis encephalitis virus; eastern, western, and Venezuelan equine encephalitis viruses; California (La Crosse) virus; and Rocio virus) and one by ticks (Powassan virus). St Louis encephalitis (SLE), eastern equine encephalitis (EEE), western equine encephalitis (WEE), Venezuelan equine encephalitis (VEE), and Rocio viruses are responsible for both endemic and epidemic disease, whereas California encephalitis (CE) and Powassan viruses cause sporadic, endemic infections. Unique aspects of arboviral encephalitis in the Americas are that several viruses (EEE, WEE, VEE) afflict equines and that during outbreaks equine morbidity and mortality generally exceeds by tenfold or more that in man. Outside the Americas, other mosquito-borne viruses (e.g., Japanese encephalitis and West Nile viruses) occasionally produce sporadic or epizootic disease in horses, but the equine disease is at present of much less epidemiological importance than the human infections.

The most complete information regarding incidence of arboviral encephalitis has been accumulated in the United States of America because of the high level of

* The situation concerning arthropod-borne encephalitides in other parts of the world will be covered in later issues of the *Bulletin*.

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surveillance and laboratory diagnosis. Between 1955 and 1978, 6970 human cases of arboviral encephalitis of known etiology were reported to the Center for Disease Control (CDC), Atlanta, Georgia, USA. In most years, however, only 25–50% of clinical encephalitis cases occurring in the USA are etiologically defined, and arboviruses undoubtedly account for a higher disease incidence than official reports indicate. Table 1 shows the distribution of human arboviral encephalitis cases by etiology and year in the USA. SLE (4824 cases), CE (1035), and WEE (947) accounted for 98.5% of all reported infections. In the past 5 years (1974–78), important epidemics of SLE and WEE have occurred.

Table 1. Number of cases of arboviral encephalitis[a], in the United States of America, reported to the Center for Disease Control, Atlanta, Georgia, 1955–78

| Year | SLE | WEE | EEE | CE | Other | Total |
|---|---|---|---|---|---|---|
| 1955 | 107 | 37 | 15 | | | 159 |
| 1956 | 563 | 47 | 15 | | | 625 |
| 1957 | 147 | 35 | 5 | | | 187 |
| 1958 | 94 | 141 | 2 | | | 237 |
| 1959 | 118 | 14 | 36 | | | 168 |
| 1960 | 21 | 21 | 3 | | | 45 |
| 1961 | 42 | 27 | 1 | | | 70 |
| 1962 | 253 | 17 | 0 | | | 270 |
| 1963 | 19 | 56 | 0 | 1 | | 76 |
| 1964 | 470 | 64 | 5 | 42 | 1[b] | 582 |
| 1965 | 58 | 172 | 8 | 59 | | 297 |
| 1966 | 323 | 47 | 4 | 64 | | 438 |
| 1967 | 11 | 18 | 1 | 53 | | 83 |
| 1968 | 35 | 17 | 12 | 66 | 1[c] | 131 |
| 1969 | 16 | 21 | 3 | 67 | 1[c] | 108 |
| 1970 | 15 | 4 | 2 | 89 | | 110 |
| 1971 | 57 | 11 | 4 | 58 | 20[d] | 150 |
| 1972 | 13 | 8 | 0 | 46 | 3[e] | 70 |
| 1973 | 5 | 4 | 7 | 75 | | 91 |
| 1974 | 72 | 2 | 4 | 30 | | 108 |
| 1975 | 1815 | 133 | 3 | 160 | 2[f] | 2113 |
| 1976 | 379 | 1 | 0 | 47 | | 427 |
| 1977 | 169 | 46 | 1 | 69 | 4[g] | 285 |
| 1978[h] | 22 | 4 | 5 | 109 | 1[i] | 140[j] |
| Total | 4824 | 947 | 136 | 1035 | 33 | 6970 |

[a] SLE = St Louis encephalitis; EEE = Eastern equine encephalitis; WEE = Western equine encephalitis; CE = California encephalitis.
[b] Tensaw encephalitis.
[c] Venezuelan equine encephalitis (VEE).
[d] 19 cases of VEE; 1 of Powassan encephalitis (POW).
[e] 2 cases of VEE (both imported), 1 of POW.
[f] Powassan encephalitis.
[g] 3 cases POW; 1 of VEE.
[h] 1978 data for SLE are preliminary.
[i] 1 case of POW.
[j] 1978 data preliminary.

Estimates of equine morbidity associated with arboviral infections in the USA are less accurate. Table 2 shows the annual incidence of clinical encephalitis in horses and mules from 1935 to 1972. In the last three decades approximately 1000–4000 cases have been notified annually; the incidence has remained similar from year to year despite a declining equine population. Since 1956, efforts have been made to achieve specific etiological diagnoses. Of 3302 cases provisionally identified by laboratory tests (usually demonstration of antibodies in a single serum sample), 2471 have been due to WEE, 684 to EEE, and 147 to VEE viruses. In the state of Florida, an active surveillance programme resulted in the diagnosis of 286 EEE infections among 1758 reported clinical cases of equine encephalitis occurring between 1955 and 1974.

In Central and South America, outbreaks of EEE and Rocio encephalitis have occurred in several localities during the last five years (Fig. 1). In addition, equine epizootics (generally without recognized associated human cases) were reported in Brazil, Colombia, Costa Rica, Guyana, and Venezuela, without definition of specific etiology. VEE or EEE viruses were probably responsible for these outbreaks.

Research activities in the past few years resulted in new information about the epidemiology and ecology of the arboviral encephalitides. In this brief review, the recent impact of each disease will be assessed and the highlights of current research accomplishments in the area of disease ecology are presented. A brief summary of the basic epidemiology of each virus is given as an introduction to the disease.

Table 2. Morbidity and mortality due to encephalitis in Equidae in the United States of America, 1935–72, compiled by the Animal and Plant Health Inspection Service, US Department of Agriculture

| Year | Estimated equine population[a] | Number of cases | | | | Encephalitis (per 1000 equines) | No. of Deaths | Case fatality rate (%) |
|---|---|---|---|---|---|---|---|---|
| | | Total encephalitis[b] | Etiology defined[c] | | | | | |
| | | | EEE | WEE | VEE | | | |
| 1935 | 16 683 000 | 23 512 | — | — | — | 1.4 | — | — |
| 1936 | 16 226 000 | 3 929 | — | — | — | 0.2 | — | — |
| 1937 | 15 802 000 | 173 889 | — | — | — | 11.0 | — | — |
| 1938 | 14 245 000 | 184 662 | — | — | — | 12.1 | — | — |
| 1939 | 14 792 000 | 8 008 | — | — | — | 0.5 | 2 471 | 31 |
| 1940 | 14 481 000 | 16 941 | — | — | — | 1.2 | 4 187 | 25 |
| 1941 | 14 136 000 | 36 872 | — | — | — | 2.6 | 8 210 | 22 |
| 1942 | 13 720 000 | 4 939 | — | — | — | 0.4 | 1 334 | 27 |
| 1943 | 13 379 000 | 4 768 | — | — | — | 0.4 | 1 622 | 34 |
| 1944 | 12 833 000 | 19 599 | — | — | — | 1.5 | 4 779 | 24 |
| 1945 | 12 246 000 | 3 212 | — | — | — | 0.3 | 1 165 | 36 |
| 1946 | 11 455 000 | 2 805 | — | — | — | 0.2 | 957 | 34 |
| 1947 | 10 129 000 | 8 716 | — | — | — | 0.9 | 5 086 | 58 |
| 1948 | 9 279 000 | 1 796 | — | — | — | 0.2 | 635 | 35 |
| 1949 | 8 498 000 | 4 037 | — | — | — | 0.5 | 2 426 | 60 |
| 1950 | 7 781 000 | 1 023 | — | — | — | 0.1 | 417 | 41 |
| 1951 | 7 036 000 | 762 | — | — | — | 0.1 | 274 | 36 |
| 1952 | 6 150 000 | 2 226 | — | — | — | 0.4 | 898 | 40 |
| 1953 | 5 403 000 | 2 813 | — | — | — | 0.5 | 827 | 29 |
| 1954 | 4 791 000 | 1 075 | — | — | — | 0.2 | 357 | 33 |
| 1955 | 4 309 000 | 1 236 | — | — | — | 0.3 | 663 | 54 |
| 1956 | 3 928 000 | 1 284 | 41 | 35 | — | 0.3 | 493 | 38 |
| 1957 | 3 574 000 | 1 525 | 29 | 44 | — | 0.4 | 639 | 42 |
| 1958 | 3 354 000 | 2 054 | 19 | 112 | — | 0.6 | 494 | 24 |
| 1959 | 3 079 000 | 817 | 95 | 7 | — | 0.3 | 324 | 40 |
| 1960 | 2 982 000 | 813 | 18 | 31 | — | 0.3 | 252 | 31 |
| 1961 | 2 889 000 | 781 | 10 | 31 | — | 0.3 | 245 | 31 |
| 1962 | 2 780 000 | 734 | 1 | 23 | — | 0.3 | 141 | 19 |
| 1963 | 2 710 000 | 2 426 | 23 | 39 | — | 0.9 | 162 | 7 |
| 1964 | 2 625 000 | 3 950 | 12 | 281 | — | 1.5 | 392 | 10 |
| 1965 | 2 543 000 | 4 391 | 46 | 383 | — | 1.7 | 705 | 16 |
| 1966 | 2 463 000 | 2 123 | 84 | 302 | — | 0.9 | 291 | 14 |
| 1967 | 2 385 000 | 965 | 11 | 177 | — | 0.4 | 163 | 17 |
| 1968 | 2 311 000 | 1 627 | 132 | 272 | — | 0.7 | 317 | 19 |
| 1969 | 2 238 000 | 1 767 | 35 | 211 | — | 0.8 | 681 | 39 |
| 1970 | 2 092 000 | 1 211 | 49 | 67 | — | 0.6 | 321 | 27 |
| 1971 | 1 955 000 | — | 47 | 4 | 147[d] | — | — | — |
| 1972 | 1 827 000 | — | 32 | 452 | 0 | — | — | — |
| Total | — | 533 288 | 684 | 2 471 | 147[d] | — | 41 928 | — |

[a] Based on US Department of Agriculture census data and intercensal estimates from 1935 to 1959, when last enquine census was conducted in the United States, and on estimated equine population data obtained in 1969 and 1974. Only farm animals are included.

[b] Clinical cases of encephalitis in Equidae.

[c] A dash indicates that no information is available.

[d] It has been estimated that as many as 1528 fatal cases of VEE in Equidae occurred in Texas in 1971.

## SAINT LOUIS ENCEPHALITIS

St Louis encephalitis (SLE) virus causes an acute illness in man, with a spectrum of central nervous system (CNS) manifestations from self-limited fever with headache to fatal meningoencephalitis, but is not pathogenic for equines. The virus is a member of the *Flavivirus* genus, family Togaviridae. It is distributed widely from Argentina to Canada. In the USA, SLE occurs as an endemic (occasionally epidemic) disease west of the Mississippi River; in the eastern part of the USA, it periodically reappears in epidemic form, especially in the Mississippi–Ohio riverine basin, eastern Texas, and central Florida. Outbreaks have also occurred in Canada and northern Mexico. The disease incidence and severity during epidemics affecting populations with low rates of acquired immunity are greatest in the older age groups (persons over 50 years).

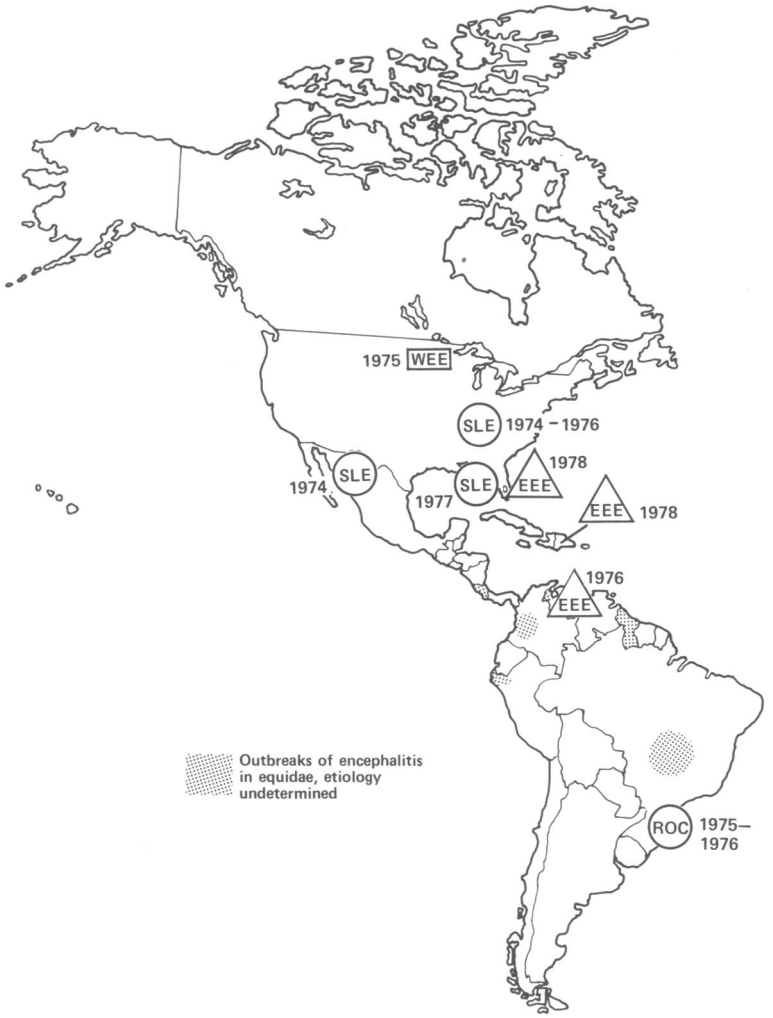


Fig. 1. Location of arboviral encephalitis outbreaks in the Americas, 1974–78.

In Central and South America, human infections (as determined by serological surveys) are frequent, but epidemics are unknown, and fewer than 25 clinical cases, many with only nonspecific syndromes, have been recognized since 1953.

In the eastern USA, the principal vectors of SLE virus are mosquitos of the *Culex pipiens* complex (*C. p. pipiens* and *C. p. quinquefasciatus*), which oviposit in polluted water and attain high population densities in urban–suburban environments. In Florida, the tropical mosquito *C. nigripalpus* is the epidemic vector. In the western USA, *C. tarsalis* transmits SLE virus; this species breeds in irrigated or in flooded dryland areas, and its wide distribution leads to frequent exposures in rural areas. Of the 4824 human cases recorded between 1955 and 1978 in the USA, approximately 75% occurred in areas where *C. p. pipiens* or *C. nigripalpus* were responsible for transmission.

Wild birds constitute the major vertebrate host in the enzootic cycle and in viral amplification that precedes "spill-over" of the virus to man. In temperate areas, viral

transmission ceases during the winter. The mechanisms of SLE viral overwintering are not clearly defined, despite recent observations (see below).

## Recent outbreaks

After a quiescent period of 8 years, SLE reappeared in epidemic form in 1974. In northwestern Mexico an epidemic of SLE occurred in August and September, 1974. The affected town, Hermosillo, is situated in an area characterized by extensive agricultural irrigation; a previous outbreak of meningoencephalitis of undetermined etiology occurred in 1972, and a serological survey in 1960 had demonstrated SLE antibodies in 13.7% of the population. In 1974, 51 hospitalized cases were recorded, with an attack rate of 19 per 100 000 inhabitants and a case-fatality rate of approximately 20%. Cases in males exceeded those in females, and the incidence in children was higher than in adults, a pattern typical of *C. tarsalis*-borne SLE in endemic areas of the western part of USA. In 1974, outbreaks of 8–50 serologically identified cases also occurred in Memphis, Tennessee, Birmingham, Alabama, and in northwestern Mississippi. A high level of viral activity in the summer, which continued in the eastern states in each of the succeeding three years, suggested that the virus was maintained in local winter reservoirs. In 1975, the most intense and geographically extensive epidemic on record occurred, and 1815 cases were reported. The area most severely affected was the Ohio–Mississippi River basin, particularly the states of Illinois, Indiana, Kentucky, Mississippi, Ohio, and Tennessee (Fig. 2). The 22 cases occurring in Ontario represented the first recognition of

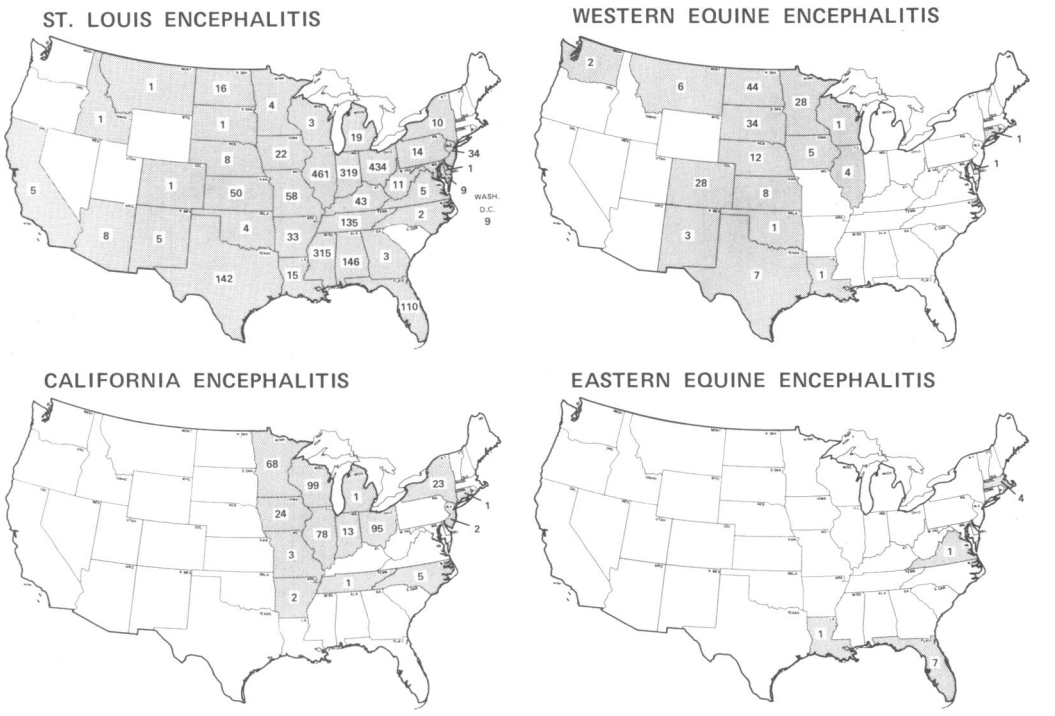


Fig. 2. Etiology and geographical distribution of human arboviral, central nervous system infections diagnosed by laboratory tests in the United States of America, 1955–78.

the disease in Canada. Outbreaks occurred in several localities in 1976, with a nationwide total of 379 cases. In 1977, 110 cases were reported from central Florida, USA.

Table 3 lists selected localities affected between 1974 and 1977, the number of cases and deaths attributed to SLE, attack and mortality rates/100 000 population, and case-fatality rates.[a] Attack rates ranged from 1.2 to 151.3/100 000, mortality rates from 0 to 22.7/100 000, and case-fatality rates from 0 to 19.4% in the various outbreaks. As in previous epidemics in the eastern USA, the attack and mortality rates increased with age. The incidence of disease and death due to SLE was 10–100 times higher in persons over 60 years of age than in those under 20 years. A serological survey in Memphis conducted in 1977 showed that approximately 6% of the population had acquired the infection during the outbreaks of 1974–1976, with an inapparent: apparent infection ratio of 355:1.

Table 3. Epidemiological parameters of selected outbreaks of St Louis encephalitis in the United States of America, 1974–77

| Year | Locality | Population | No. of laboratory documented cases | Attack rate (per 100 000) | No. of laboratory documented deaths | Mortality (per 100 000) | Case fatality rate (%) |
|---|---|---|---|---|---|---|---|
| 1974 | Memphis, TN | 760 000 | 50 | 6.6 | 5 | 0.7 | 10.0 |
| 1974 | Birmingham, AL | 649 300 | 8 | 1.2 | 0 | — | — |
| 1975 | Memphis, TN | 767 000 | 62 | 8.1 | 12 | 1.6 | 19.4 |
| 1975 | Louisville, KY | 723 300 | 27 | 3.7 | 1 | 0.1 | 3.7 |
| 1975 | Houston, TX | 2 078 000 | 30 | 1.4 | 2 | 0.1 | 6.7 |
| 1975 | Greenville, MS | 39 648 | 60 | 151.3 | 9 | 22.7 | 15.0 |
| 1975 | Cuyahoga Co. (Cleveland), OH | 1 721 300 | 83 | 4.8 | 8 | 0.5 | 9.6 |
| 1975 | Franklin Co. (Columbus), OH | 833 249 | 142 | 17.0 | 11 | 1.3 | 7.7 |
| 1975 | Chicago, IL | 6 978 947 | 322 | 4.6 | 25 | 0.4 | 7.8 |
| 1976 | Tuscaloosa, AL | 85 875 | 22 | 25.6 | 0 | — | — |
| 1977 | Florida | 6 789 443 | 110 | 1.6 | 8 | 0.1 | 7.3 |

Many isolations of SLE virus were made from mosquitos during these recent epidemics; these confirmed the vector roles of the *C. pipiens* complex in the east-central USA and eastern Texas and of *C. nigripalpus* in Florida. Table 4 shows the numbers of strains isolated and the minimum field infection rate/1000 mosquitos of each species. An important observation was the recovery of SLE virus from *C. salinarius* and *C. restuans* during the Chicago and Memphis outbreaks. These nondomestic species, especially *C. salinarius*, may play an important role in sylvan enzootic transmission of SLE virus. *C. restuans* populations reach a peak during the relatively cool spring and fall months. In Memphis, a virus isolation from this mosquito species was made in May 1975, suggesting that this species may be important in overwintering and early spring amplification, a possibility that certainly warrants further investigation.

In several areas of the eastern USA, efforts were focused on using sentinel chickens or wild-caught birds to provide serological evidence of an impending human outbreak. Serological conversions in sentinel chickens or increases in prevalence or geometric mean

[a] MONATH, T. P. ed. *Saint Louis encephalitis*. Washington, DC, American Public Health Association, 1979.

Table 4. Number of isolations of St Louis encephalitis virus from, and minimum infection rates in, mosquitos collected during epidemics in the United States of America, 1974–77[a]

| Mosquito species | Epidemic localities | No. of times virus isolated | Minimum infection rate (per 1000 mosquitos) |
|---|---|---|---|
| *Culex pipiens* complex | Ohio, Tennessee, Mississippi, east Texas, 1974–76 | 332 | 5.6 |
| *Culex salinarius* | Ohio, Tennessee, Mississippi, east Texas, 1974–76 | 15 | 13.4 |
| *Culex restuans* | Ohio, Tennessee, Mississippi, east Texas, 1974–76 | 14 | 1.8 |
| *Culex territans* | Ohio, Tennessee, Mississippi, east Texas, 1974–76 | 1 | 0.5 |
| *Culex erraticus* | Ohio, Tennessee, Mississippi, east Texas, 1974–76 | 2 | 0.2 |
| *Culex nigripalpus* | Florida, 1977 | 12 | 0.2 |

[a] Data from Vector Ecology Branch, Vector-Borne Disease Division, Center for Disease Control, Fort Collins, Colorado.

titres of haemagglutination-inhibiting (HI) antibodies in wild house sparrows (*Passer domesticus*) were noted 2–8 weeks before the first human case occurred in Memphis, several localities in Mississippi, and in Texas. In 1977, seroconversions in sentinel birds were noted 1 month before the first human cases in Florida, but antibodies in wild birds appeared late. Instead, early evidence of SLE viral activity was detected in small mammals (racoons, opossums), which suggests that they may play a role in the enzootic cycle in Florida.

The reasons for the major upsurge of SLE during the mid-1970s are not completely understood. Undoubtedly, the increase in urban–suburban human populations, with man-modified environmental changes favouring *C. pipiens* breeding, is an important element and it is disturbing to realize that vector abatement has not kept pace with this socioeconomic growth. Other factors that might influence the occurrence of SLE epidemics, including relative pathogenicity of viral strains, changes in the vector competence of mosquito populations, and vector population density require further study. Recrudescence of epidemics in successive years may depend upon the quantitative success of the overwintering mechanisms, but these mechanisms remain unclear.

## Current research

Considerable recent interest has been focused upon the question of overwintering. Workers at the Walter Reed Army Institute of Research, Washington, DC, have repeated isolations of SLE virus from hibernating adult female *Culex pipiens pipiens* mosquitos collected from abandoned ammunition bunkers in Maryland.[b] Mark-release-recapture studies conducted in these bunkers appear to show that blood-fed *C. p. pipiens* are capable of prolonged survival in hibernation, presumably because the mosquitos undergo gonotrophic dissociation as an expression of facultative reproductive diapause. Infected nulliparous adult female *C. p. pipiens* could emerge in the spring and transmit SLE virus, thereby re-establishing the active cycle.

[b] BAILEY, C. L. ET AL. Isolation of St. Louis encephalitis virus from overwintering *Culex pipiens* mosquitoes. *Science*, **199**: 1346-1349(1978).

Mitchell et al.[c] recently described bird-to-bird transmission of SLE virus by *C. p. pipiens* which had ingested volumes of infective blood too small to initiate oogenesis. These studies provide a possible mechanism other than gonotrophic dissociation to explain overwintering of SLE virus, since partially blood-fed, nulliparous infected mosquitos, which subsequenly prepared for hibernation by taking a carbohydrate meal, would have winter survival advantages.

The question of transovarian transmission of SLE virus is being actively reinvestigated because of reports of successful inherited transmission of other flaviviruses in *Aedes* mosquitos.

Differences in virulence between laboratory strains of SLE virus of diverse biological and geographical origin have been recently described and continue to be actively studied. Apparently, some strains are relatively nonpathogenic and produce low viraemia in avian hosts. The epidemiological significance of SLE viral strain variation remains to be defined; rates of virus transmission in the bird–mosquito cycle and clinical expression of disease in man may perhaps be positively influenced by selection of viral strains with enhanced pathogenicity.

## VENEZUELAN EQUINE ENCEPHALITIS

The epidemiology of Venezuelan equine encephalitis (VEE) is complicated by the existence of a number of serotypes. At present at least four subtypes of VEE virus (an *Alphavirus,* Family Togaviridae) are separable on the basis of serological and physicochemical tests. Within subtype I, four antigenic variants may be similarly distinguished, designated IAB, IC, ID, and IE. VEE IAB and IC viruses have been isolated during equine epizootics and shown to be more pathogenic for horses and man than the enzootic variants ID and IE and subtypes II, III, and IV. Epizootic VEE viruses typically cause an acute influenza-like illness in man; encephalitic illness occurs in only about 4% of infected young persons (under the age of 15 years) but has a case-fatality rate of about 20%. Equines also develop a spectrum of disease, from inapparent infection with fever to fatal encephalitis. The enzootic strains (ID, IE, II, and III) may occasionally produce sporadic disease, but have reduced virulence for equines and man.

The epizootic VEE virus strains are distributed and presumably maintained in the north of South America (Colombia, Ecuador, Guyana, and Venezuela), where outbreaks occur at intervals sufficiently long for susceptible equine populations to accumulate. In 1969, however, VEE IAB virus appeared in Guatemala and spread in epizootic waves, reaching northward to southern Texas (1971) and south to Costa Rica (1970).

Equines are the most important viraemic host; biological transmission is effected by a wide variety of mosquitos, principally belonging to the genera *Aedes, Mansonia, Psorophora.* Because of the high viraemias in equines, mechanical transmission (by *Simulium,* and other biting arthropods) is possible. Man-mosquito-man transmission and contact spread from person-to-person may play a role, but are epidemiologically of minor importance.

Enzootic VEE viruses are perennially active in subtropical and tropical areas of the Americas (subtype II in Florida; IE in Central America; ID in Panama and northwestern South America; III and IV in northeastern South America). Most of these viruses have

[c] MITCHELL, C. J. ET AL. St. Louis encephalitis virus transmission following multiple feeding of *Culex pipiens pipiens* during a single gonotrophic cycle. *Journal of medical entomology* (in press, 1979).

small rodent and marsupial hosts and are transmitted by *Culex* (*Melanoconion*) mosquitos; birds are implicated as hosts for at least one variant of subtype III.

The source of virus during epizootics remains uncertain, because there is little evidence to support an enzootic maintenance cycle of the epizootic virus variants. In some areas of South America, the use of formalinized vaccines containing residual live virus may have been responsible for initiating disease outbreaks.

## Recent outbreaks

The outbreaks of 1969–72 involving Central America, Ecuador, Mexico, Peru, and south Texas have been extensively reviewed elsewhere.[d] This unprecedented epizootic activity has been followed by a quiescent interval. Relatively minor equine outbreaks, possibly due to VEE, occurred during 1977 in Guyana, northern Peru, and the Guajira Peninsula of Venezuela.

In the United States of America, the enzootic subtype II (Everglades virus) has caused sporadic cases of undifferentiated febrile illness and meningitis in south Florida, recognized first in 1968. In 1977, a German tourist visiting the Everglades National Park acquired the disease, and virus was isolated from his blood.

## Current research

Current research on the ecology of VEE has focused on the question of the origin of epizootics, on the role of vertebrates other than equines in the cycle, and on the virus–vector relationships of enzootic subtypes in Central and South America.

In 1969, epizootic (IAB) virus appeared in an area of Guatemala that harboured only the enzootic subtype IE virus in the preceding year. This suggested either introduction from afar (possibly Ecuador or Peru, where an epizootic was in progress) or *de novo* origin of epizootic virus from the enzootic strains, by mutation or selection. Since 1970, Scherer and his colleagues, using sentinel animals, have conducted surveillance for epizootic virus strains in various parts of Central America. No clear evidence for persistence of an epizootic VEE virus maintenance cycle has been obtained. The sensitive technique of absorption chromatography, however, is now being used in attempts to find minority populations of epizootic virions in field isolates of enzootic strains. In addition, guinea pigs, which develop lethal infection with subtype IAB and IC virus strains but not subtype IE virus, are being used as sentinel animals to detect equine-virulent virus in natural habitats. It is still too early to assess whether a process of mutation and/or selection accounts for epizootic VEE viral persistence and recrudescence.

The role of birds in enzootic virus transmission or in dissemination of epizootic virus remains conjectural. Experimental transmission has been demonstrated between birds and *Culex (Melanoconion) aikenii, nom. dub.*, the primary enzootic vector in Panama, where a high frequency of natural blood feedings by *C. (M.) aikenii* upon birds has been reported. Particularly in the case of *C. (M) aikenii*-borne VEE, water-birds probably represent an important element of the transmission cycle. Experimental studies aimed at investigating the participation of birds in VEE virus transmission cycles have recently provided evidence that many species, particularly ciconiiform birds, develop brief

[d] *Venezuelan encephalitis*, Washington, DC, Pan American Health Organization, 1972, (Scientific Publication, N° 243).

viraemias of sufficient titre to infect vector mosquitos. A role for certain birds in long-range transport of epizootic viral variants remains a possibility.

Recently, a new virus (Tonate), apparently a variant of subtype III, was isolated from wild birds captured in French Guiana and Suriname, and a closely related strain (Bijou Bridge virus) has been recovered from nestling house sparrows and ectoparasitic bugs in the western USA. Tonate virus may be primarily bird-associated, a unique attribute for a member of the VEE virus complex. These is not yet any evidence of public health importance; the Bijou Bridge strain from the USA has low pathogenicity for experimentally inoculated horses.

Bats have been implicated as potential hosts for both epizootic and enzootic VEE viruses, but their role in transmission cycles is in doubt. Recent reports by Seymour and colleagues[e] indicate that *Artibeus* bats may be important hosts (secondary to rodents and marsupials) in the long-term maintenance of enzootic VEE IE virus.

In the past few years, our knowledge of the vector relationships of the Central and South American enzootic variants, IE and ID, has expanded. *C. (M.) aikenii* is a principal vector in Panama and probably elsewhere in South America. The ecological associations of this species, which breeds in water lettuce (*Pistia*) colonies in rivers, lakes, and lagoons, have provided important insights into the distribution and seasonal patterns of VEE activity. In Guatemala and probably elsewhere in Central America, *C. (M.) opisthopus* appears to be an important vector of VEE. This mosquito is also apparently responsible for transmission of enzootic VEE (subtype II) virus in south Florida.

## EASTERN EQUINE ENCEPHALITIS

Eastern equine encephalitis (EEE) virus (an *Alphavirus*) causes acute encephalitis in equines and man, especially children, in whom high case-fatality and low inapparent: apparent infection ratios are described. In the USA, equine cases occur each summer along the Gulf and Atlantic coasts and occasionally inland in the eastern half of the country. Cases in eastern Canada were first recorded in 1972. The epidemiological pattern of equine disease is generally one of sporadic dispersed infections, and human cases are rare; 136 human cases have been reported since 1955 (Table 1). The July through October transmission cycle in freshwater swamp habitats involves wild birds and the aviaphilic vector, *Culiseta melanura,* which only rarely feeds upon horses and man. Fortunately, equine epizootics and human epidemics have been unusual events in the USA; outbreaks are associated with infection of abundant agressive vectors, such as *Aedes sollicitans* and *Aedes vexans.* Epornitic outbreaks in penned exotic birds (pheasants, chukar partridges) are also caused by EEE virus (transmitted from bird to bird by pecking and cannibalism), but this problem has been successfully reduced in many areas by vaccination.

The overwintering mechanism of EEE in North America is unknown. *Culiseta melanura* overwinters in the larval stage and on one occasion the virus was isolated from larvae. Transovarian transmission has been suggested, but recent field and laboratory studies have not supported this concept.

Panama, Trinidad, and the northern part of South America from Brazil to Venezuela are subject to periodic epizootics of EEE; associated human cases are infrequent. EEE

[e] SEYMOUR, C. ET AL. Venezuelan encephalitis virus infection in neotropical bats. I. Natural infection in a Guatemalan enzootic focus. *American journal of tropical medicine and hygiene,* **27**: 290-296 (1978).

virus has also caused occasional equine outbreaks in the coastal Saõ Paulo State of Brazil, where the virus is apparently not perennially active and may be periodically reintroduced. In some areas, such as north-central Argentina and Guyana, mixed outbreaks of EEE and WEE, or of EEE-WEE-VEE have been reported. The virus–vector relationships of epizootic EEE in tropical America are poorly understood; in Trinidad and Brazil *Culex taeniopus* is a recognized enzootic vector.

The Caribbean is also a receptive zone, and sporadic epizootics have affected Cuba, Hispaniola, and Jamaica. These outbreaks are caused by the North American serotype of EEE virus, distinguishable by the short-incubation HI test from South American strains. In the autumn, virus seeding of the Antilles by birds migrating southward from the USA seems plausible, but the question of indigenous enzootic maintenance cycles in the islands requires further study.

**Recent outbreaks**

An outbreak of EEE in horses involved two northeastern States of the USA (Massachusetts and New Hampshire) in 1973; 122 horses died, and 28 of these deaths were confirmed by laboratory tests as having been caused by EEE. Two confirmed nonfatal human cases were recognized, both in Massachusetts. In 1974 and 1975, 4 fatal human cases occurred in the State, but there were no equine deaths, possibly because of the success of an equine vaccination campaign in 1973. The sentinel value of equine deaths was thus lost in 1974–75. Vector surveillance revealed that, in 1973, the minimum EEE virus infection rate from mosquitos (1.42 per 1000) was at least 20 times higher than in nonepidemic year.

Between February and June 1976, an outbreak of encephalitis in equines occurred in the municipality of San Carlos, Colon District, Zulia State, Venezuela. EEE virus had previously been recovered from a sentinel hamster in this area in 1975, but was isolated for the first time in Venezuela from the brain of a sick horse in March 1976. One hundred and twelve cases in Equidae were reported, with 69 deaths. The outbreak occurred in an area where VEE virus was also known to be active. No associated human infections were recognized.

In 1976, an extensive equine outbreak occurred in upstate New York (in an area southwest of Lake Ontario), and 37 cases were confirmed by laboratory tests. Eight strains of EEE virus were obtained from *Culiseta melanura* (minimum field infection rate 2.5 per 1000 mosquitos), and 16.2% of wild birds in the area had HI antibodies. No isolates were obtained from *Aedes* mosquitos, suggesting that the enzootic vector caused the virus spill-over to equines.

Between January and March 1977, equine cases occurred in Guyana. Initially, this was apparently an outbreak of mixed etiology, with infections attributed to EEE, WEE, and VEE viruses, but in March, only EEE infections were found.

In mid-February 1978, an equine epizootic was recognized in the provinces of María Trinidad Sánchez and Samaná, northeastern Dominican Republic. One hundred and twenty-three fatal equine cases were reported in early April, and EEE virus (North American serotype) was isolated from the brains of two horses. A combined equine vaccination and spray insecticide control programme was undertaken during the outbreak. The vector was not established, but *Culex nigripalpus* was the predominant species collected during investigations in April, whereas neither *Aedes sollicitans* nor *A. taeniorhynchus* (implicated in past outbreaks in the Dominican Republic) were collected.

EEE viral activity was also higher than usual in the southeastern parts of the USA in 1978. In Florida, 121 equine and 5 human cases were recorded from 14 counties. Serological conversions were found in sentinel chickens, and EEE virus isolations were obtained from pools of *Culiseta melanura.*

### Current research

Little substantive recent progress has been made in the elucidation of EEE virus epidemiology and ecology.

## WESTERN EQUINE ENCEPHALITIS

Western equine encephalitis (WEE) virus causes acute meningoencephalitis in horses and man; the disease is especially severe in infants and young children. Sporadic cases are recognized annually, but at irregular intervals outbreaks appear which may involve thousands of horses and hundreds of human subjects. Since 1955, 947 human cases have been officially reported in the USA—186 within the past 5 years. The case-fatality rate is approximately 3–4%. The disease is confined almost exclusively to the western states (Fig. 2), and only sporadic cases in the east are known, yet high rates of infection with a virus closely related to WEE are found annually in mosquito vectors in the eastern USA. Two factors underlie these observations: (1) the vector in the western USA is *Culex tarsalis,* a species that is widespread in irrigated agricultural areas and which readily bites man, whereas in the eastern USA, WEE virus is transmitted by *Culiseta melanura,* a highly aviaphilic species present in freshwater swamp habitats; (2) virus strains from the eastern USA appear to differ serologically and in certain physicochemical and genetic markers, and probably have reduced pathogenicity for horses and humans.

WEE viral activity reaches a peak in the early summer and midsummer in the *C. tarsalis* and *Culiseta melanura* transmission cycles. Wild birds, especially nestlings, constitute the enzootic and amplifying vertebrate link in the cycle. The rate of viral transmission, and consequently the risk of human infection, can be quantitatively assessed by measuring vector population density, incidence of nestling bird viraemias, serological conversions of sentinel fowl, and by other techniques. These surveillance parameters are useful for prediction. Equine epizootics generally precede the appearance of human cases, but horses play no role in the transmission cycle. In parts of western Canada (Alberta, Saskatchewan), epizootics have occurred in areas where *C. tarsalis* is relatively scarce; the cold-weather adapted species, *Culiseta inornata,* is a suspected vector in these areas. A secondary cycle of transmission involving *Aedes melanimon* mosquitos and jack rabbits has been described in the western USA. The overwintering mechanisms have not been established.

WEE virus has been isolated in eastern South America (Argentina, Brazil, Guyana, Uruguay), where it is responsible for some equine morbidity. The available information suggests that epizootics are usually of mixed (EEE-WEE or VEE-EEE-WEE) etiology in these areas; associated human cases have been rare or absent. WEE has not been isolated in Central America, where a recent serological survey also indicates that infections are extremely rare. The vector relationships in South America are virtually unknown.

**Recent outbreaks**

The only notable outbreaks in recent years occurred in 1975 in the Red River Valley of North Dakota, in Minnesota, in South Dakota, and in adjacent areas of Manitoba, Canada. The outbreak was precipitated by extensive flooding in the early summer, which provided favourable breeding conditions for *C. tarsalis*. In North Dakota–Minnesota, USA, the equine outbreak began in early July, reached a peak in late July–early August, and subsided rapidly in mid-August. Human cases appeared 2–3 weeks after equine cases, and the highest incidence of disease was no more than 10 days after the equine epizootic peak. As in other outbreaks transmitted by *C. tarsalis*, cases of SLE occurred, although WEE predominated. Three hundred and forty-six suspect human cases were identified, and 45 were documented by laboratory tests to be WEE, 13 to be SLE. The attack rate for WEE in males (7.7/100 000) was higher than that in females (1.6); this indicates increased male exposure to the vector during farming and recreational pursuits. The human disease was characterized by a spectrum of severity from fever with headache to fatal encephalitis; the overall case-fatality rate was 7.7 %. Equine morbidity estimated by active surveillance methods was 281 cases, with a minimum of 18 deaths. A prospective serological survey in one affected county showed that 1.7 % of the population was infected with WEE virus and 0.2 % with SLE virus between August and October, 1975. Over 400 isolations of WEE virus were made from *C. tarsalis*, the incriminated vector. Infection rates for WEE and SLE, respectively, were 2.0 and 0.61/1000 *C. tarsalis*.

The outbreak in Manitoba, Canada, has been reviewed in detail elsewhere.[f] Seroconversions of sentinel chickens were detected in mid-June. The first clinically suspect equine case occurred on 5 June; between then and 1 August, 19 equine cases were recorded. The epizootic reached a peak in the second week of August. Recorded equine cases totalled 261, with an approximate morbidity rate of 870/100 000 horses. Surveillance activities revealed 196 suspect human cases, only 14 of which were confirmed as WEE. There were no deaths, but 4 patients had neurological sequelae. Important factors in precipitating the Manitoba outbreak were abnormally high precipitation and high mean weekly temperature during the early summer favouring *C. tarsalis* breeding. Light-trap collections between June and September indicated a high relative abundance of *C. tarsalis* compared with nonepidemic years.

**Current research**

The antigenic differences described previously by Karabatsos and Henderson between strains of WEE virus associated with the *C. tarsalis* cycle in the western USA and the *Culiseta melanura* cycle in the east have been confirmed by various serological methods, including use of antisera prepared against the individual viral glycoproteins. Strains from South America appear to be similar to those from the western USA. Similarly, fingerprinting of the viral RNA oligonucleotides has shown that genome homology correlates with the serological relationships (D. Trent and C.H. Calisher, personal communication, 1979). Different strains from each region have minor differences in RNA fingerprints, but when multiple strains from a single outbreak (e.g., North Dakota–Minnesota) were examined, identical patterns were obtained. This technique provides a sensitive novel epidemiological tool in determining the origin of

[f] SEKLA, L. H., ed., Western encephalomyelitis. *Canadian journal of public health*, **67** (Special Supplement): 1-75 (1976).

outbreaks. Differences between WEE virus strains from the western and eastern USA appear to be so marked that it no longer seems tenable to designate them as a single virus. The separate nomenclature and methodology for typing are especially relevant to surveillance activities in areas of the central USA where the *C. tarsalis* and *Culiseta melanura* cycles interface.

An interesting recent observation has been the isolation of a new agent, Fort Morgan virus, from cimicid bugs (*Oeciacus vicarius*) in the western USA. The virus is closely related antigenically to WEE virus, and is transmitted in a cycle involving the bugs and nestling cliff swallows and house sparrows.[g] Overwintering has been documented to occur by means of infected hibernating nymphal and adult bugs which remain in bird nests throughout the year. Fort Morgan virus is apparently nonpathogenic for equines and does not infect mosquitos. Although these findings have little direct relevance to WEE epidemiology, they do illustrate the possible role of vectors other than mosquitos as winter virus reservoirs.

Perhaps the most important recent research development is the investigation by Hardy and coworkers of the competence of *C. tarsalis* as a WEE viral vector.[h] *C. tarsalis* field and colony populations of different geographical origin were compared for susceptibility to WEE virus. All were uniformly susceptible to infection after intrathoracic inoculation, but marked differences in infection rates were noted after oral ingestion over a wide dose range. The physiological mechanisms determining the mesenteronal barrier are now being intensively studied, but it is clear[i] that viral susceptibility is a genetically determined trait. These studies pave the way for the use of refractory strains in biological control, and also provide possible leads to explain epidemiological patterns. Heritable changes in the fitness of geographical or seasonal vector populations as vectors could markedly influence rates of viral transmission, and could even be a factor in the selection of viral strains with increased pathogenic potential.

## ROCIO ENCEPHALITIS

This disease was first described in 1975. Between March and June 1975, 465 cases with 61 deaths were recorded in an outbreak involving Itanhaem, Mongaguá, and Peruibe, counties located in the coastal region of São Paulo State, Brazil.[j] The overall attack rate was 15 per 1000 population; the mortality rate 2 per 1000; and the case-fatality ratio 13%. Adult males were most severely affected, suggesting exposure out-of-doors during farm labour. Epidemics of the disease occurred also in September, 1975, and during early 1976; outbreaks in 1976 also involved the coastal area of São Paulo State, but a southward progression of the epidemic (towards Parana State) was noted. Between March 1975 and May 1976, 825 cases and 95 deaths were reported. The disease did not recur in 1977–78. The high overall attack rate, high incidence in adults, and lack of prior knowledge of a similar illness in the area suggested that the disease had been recently introduced.

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[g] HAYES, R. O. ET AL. Role of the cliff swallow bug (*Oeciacus vicarius*) in the natural cycle of a western equine encephalitis-like alphavirus. *Journal of medical entomology*, **14**: 257-262 (1977).

[h] HARDY, J. L. ET AL. Variations in the susceptibility of field and laboratory populations of *Culex tarsalis* to experimental infection with western equine encephalomyelitis virus. *American journal of epidemiology*, **103**: 498-505 (1976).

[i] HARDY, J. L. ET AL. Selection of a strain of *Culex tarsalis* resistant to infection following ingestion of western equine encephalomyelitis virus. *American journal of tropical medicine and hygiene*, **27**: 313-321 (1978).

[j] LOPES, O. DE S. ET AL. Emergence of a new arbovirus disease in Brazil. *American journal of epidemiology*, **108**: 396-401 (1978).

The etiological agent, isolated from tissues obtained at autopsy from 10 patients who died before the 5th day of illness in 1975, has been shown to be a new *Flavivirus,* antigenically distinct from other members of this genus. The transmission cycle remains unknown; available information suggests that the virus is mosquito-borne and that wild birds may be important hosts. Rocio virus has been isolated from sentinel mice exposed in the epidemic area and from a wild-caught rufous-collared sparrow. Extensive studies on mosquitos captured during the epidemics yielded a single isolation of Rocio virus from *Psorophora ferox* (O. de S. Lopes and D. B. Francy, personal communication, 1979). Experimentally inoculated house sparrows develop viraemia, but this abudant species does not appear to be an especially efficient host. In laboratory studies, *C. pipiens* and *C. tarsalis* mosquitos have transmitted the virus from chick to chick (C. J. Mitchell and T. P. Monath, unpublished observations, 1979).

The clinical and histopathological features of Rocio encephalitis have been described by Tiriba et al.[k] and Rosemberg.[l]

## CALIFORNIA ENCEPHALITIS

The California serogroup of Bunyaviruses is comprised of 12 registered viruses, of which 2, California encephalitis virus and La Crosse virus, are known to cause acute CNS disease in the Americas. California encephalitis (CE) virus has been implicated in only three human cases in California in 1945.

La Crosse virus began to be recognized as a major human pathogen in the early 1960s; between 1963 and 1978, 1035 cases were officially reported to CDC (Table 1). The epidemiological pattern of CE is endemic rather than epidemic, and the incidence varies but is usually 50–100 cases annually. The disease is most prevalent in north-central USA (Fig. 2) and primarily affects children less than 15 years of age living in rural areas characterized by deciduous hardwood forest. Cases occur between July and September, with peak incidence in August. The clinical spectrum extends from undifferentiated febrile illness to severe meningoencephalitis, which, however, is only rarely fatal (case-fatality rate less than 1%).

La Crosse virus is principally transmitted by *Aedes triseriatus* mosquitos, which breed in tree holes and occasionally in artificial containers. Small mammals, especially squirrels and chipmunks, develop viraemic infections and serve as amplifying hosts in the cycle, but the virus is also maintained in nature by a high rate of transovarian transmission in the vector. This phenomenon, which assures virus survival in diapaused eggs of the vector and springtime recrudescence of La Crosse virus, has been the subject of intensive recent research (see below).

### Recent viral activity

In 1975 and 1978, the incidence of CE in the USA was unusually high (160 and 109 cases, respectively). Cases were dispersed in the endemic zone, reflecting a widespread upsurge of enzootic viral activity; the reasons for this were not defined, but may relate to increased vector and/or susceptible vertebrate host population densities.

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[k] TIRIBA, A. ET AL. Encefalite humana primaria epidemica por arbovirus observada no litoral Sul do Estado de São Paulo. *Revista da Associacao Medica Brasileira,* **22**: 415-420 (1976).

[l] ROSEMBERG, S. Neuropathological study of a new viral encephalitis: The encephalitis of São Paulo south coast. (Preliminary report). *Revista do Instituto de Medicina Tropical de São Paulo,* **19**: 280-282 (1977).

In 1978, surveillance for the disease in Minnesota and Wisconsin revealed 54 cases. One of these cases resulted in death (of a 3-year-old girl), and La Crosse virus was isolated from brain tissue; this is only the second recorded virus isolation from man. Another death (of a 13-year-old boy) occurred in New York State in 1978. Field studies conducted during the summer in Minnesota resulted in the isolation of La Crosse virus from *A. triseriatus* (minimum field infection rate approximately 10 per 1000 mosquitos) and from eastern chipmunks (*Tamias striatus*).

## Current research

The discovery of transovarian transmission of La Crosse virus (and subsequently of six other members of the California virus group) has resulted in a burgeoning of research on the epidemiological implications of the phenomenon. A report on the isolation of La Crosse virus from *A. triseriatus* larvae collected from tree holes in Wisconsin was followed by experimental studies by Dr. D. M. Watts and his colleagues. These studies showed that La Crosse virus was transmitted through the egg to adults of the next generation. Such transmission explains in part the focality of La Crosse viral activity. In recent studies at the University of Wisconsin, prevalence levels of La Crosse virus in larvae from field-collected diapaused eggs of *A. triseriatus* were found to be between 29 and 59 per 10 000 larvae. Approximately 98% of experimentally infected female *A. triseriatus* transmitted the virus to their progeny, and in successive generations approximately 65–85% of offspring from infected female mosquitos carried the virus.[m] Since rates of detectable inherited infection are not 100%, the virus apparently cannot survive indefinitely in nature without being replenished by horizontal transmission. Although viraemic wild rodents undoubtedly contribute to this, paternal vertical transmission (by venereal infection of uninfected females by infected males) may also replenish the cycle. It is estimated that the virus can persist in an area without involvement of the mosquito–vertebrate cycle for 4 years or more. This adaptation assures survival of the virus in areas depleted of vertebrate hosts (by population crashes or natural immunization).

In the area of vector competence, Dr P.R. Grimstad and colleagues have recently studied the susceptibility of 20 strains of *A. triseriatus* to La Crosse virus. These strains differed widely in infection and transmission rates, and a geographical pattern was evident. Strains from the region hyperendemic for La Crosse virus were less competent vectors than strains from nonendemic areas, which suggests that resistance to the virus had evolved. Whether La Crosse viral infection exerts a deleterious effect on the vector has not been determined. It also remains to be investigated whether the phenomenon of transovarian transmission of virus is under genetic control and whether different rates of inherited infection in different vector populations could explain variations in viral prevalence.

Like other bunyaviruses, the California group viruses contain an RNA genome which is in three separate segments. This structure allows the possibility of genetic recombination in cells dually infected with different strains of the same viral serotype (or even with heterologous viruses). Recombination has recently been demonstrated between La

[m] MILLER, B. R. ET AL. Vertical transmission of La Crosse virus (California encephalitis group): transovarial and filial infection rates in *Aedes triseriatus* (Diptera: Culicidae). *Journal of medical entomology*, **14**: 437-440 (1970).

Crosse and snowshoe hare viruses. This mechanism may explain the known diversity of California group virus serotypes and suggests the possible evolution of new types. To identify the genetic variation of La Crosse virus, El Said et al.[11] have studied 11 isolates from various ecological niches in the USA. Nearly all strains were distinguishable by RNA oligonucleotide fingerprinting; this suggested that considerable evolution of La Crosse virus had occurred. Homology was noted between strains from a single region, and comparisons between strains of different geographical origin suggested possible bases for evolutionary trends. Further observations are needed to define the epidemiological significance of genetic recombination and strain variation.

## TICK-BORNE ENCEPHALITIS

Powassan virus is a rare cause of acute viral CNS disease in Canada and USA. The virus was first isolated from the brain of a 5-year-old boy who died of encephalitis in 1958 in Ontario, Canada. In 1970, a nonfatal case was serologically diagnosed; the patient apparently acquired the disease in Pennsylvania. Seven other cases were officially reported in the USA between 1970 and 1978; most of them were from upper New York State. The clinical manifestation is generally encephalitis, and residual neurological deficits have been described in some survivors. The virus is maintained in a cycle involving wild mammals (woodchucks, squirrels, etc.) and ixodid ticks. Transmission to man by the tick vector is a rare event, and fewer than 1 % of residents of enzootic areas have demonstrable antibodies. The virus is present in the western USA, but no clinical disease has been recognized.

In 1977, the first case of imported tick-borne encephalitis in the USA was detected in a 4-year-old girl who had acquired the disease by tick bite in Hungary.

## PREVENTION AND CONTROL OF THE ARBOVIRAL ENCEPHALITIDES

Progress in prevention and control has not kept pace with research on the more basic scientific aspects of arboviral infections. In the past decade in the Americas, major encephalitis outbreaks have occurred, some with unprecedented morbidity rates and geographical spread (in particular, the 1969–72 epizootic of VEE and the 1974–77 epidemic of SLE). Endemic diseases, such as California encephalitis, have continued to occur with unabated incidence.

Multiple factors underly this unfortunate situation. Little support is available today in the USA for applied research on vector control. Mosquito control is functionally committed to abatement districts of local health departments supported by taxation, and is often directed towards the control of pests rather than disease vectors. Other problems include the increasing resistance of vectors to licensed chemical insecticides (a significant problem in the case of *Culex tarsalis* and *C.p. pipiens*) and the intensified environmentalist concern about the detrimental effects of chemical contamination. Industrial research on the development of new chemical insecticides has also been slow. The negative

[11] EL SAID, L. H. ET AL. Comparison of La Crosse virus isolates obtained from different ecological niches in the United States, and analyses of the structural components of California encephalitis and other serogroup bunyaviruses. *American journal of tropical medicine and hygiene*, **28**: 364-386 (1979).

influence of these factors must be viewed together with the effects of man-made ecological modifications that favour high vector population densities and vector–host contacts. Increases in rural agricultural irrigation and larval habitats resulting from water resource projects and the expansion of urban environments with attendant waste-disposal and sanitation problems are two obvious examples.

On the brighter side, sophistication, both in the use of predictive surveillance of enzootic vital activity and in the means available for integrated pest control, preventative intervention, and emergency vector control, has increased. Programmes have been established in some areas to assess arboviral infection rates in mosquitos and birds, the size of adult mosquito populations, and climatic factors influencing mosquito production and behaviour and to use this information in the prediction of outbreaks. Many mosquito abatement districts and local health agencies in the USA have acquired new equipment for ultra-low volume (ULV) application of insecticides; and pesticide activities against adult mosquitos have been increasingly focused on vector species on the basis of surveillance data indicating viral activity in advance of human disease. Contingency planning for emergency vector control has improved, with the result that control measures are more rapidly taken.

Aerial and ground ULV application of insecticides has been used in nearly every recent arboviral outbreak in the USA and also, in many instances, in tropical America. The effectiveness of these measures, however, needs to be further assessed. In the WEE outbreak in North Dakota in 1975, aerial ULV spraying with malathion was begun 3 weeks after the onset of the equine outbreak and 5 days after the first human case. Spraying was limited to populated "urban" areas (population >7000) in and adjacent to the Red River Valley. The attack rate for confirmed WEE and SLE in unsprayed urban residents (12.84/100 000 population) was statistically significantly higher than that in sprayed areas (4.00/100 000).

New alternatives to the chemical control of arboviral encephalitis vectors in the Americas are under investigation and hold promise for the future. A detailed discussion of the subject is beyond the scope of this review. One approach under intensive study at the University of California, Berkeley, is the genetic modification of *C. tarsalis* by sex-linked heterozygous double chromosomal translocation. Incorporation of the genetic alteration into the wild mosquito population should result in significant reductions in vector densities and reduced rates of viral transmission. Genetic alterations influencing vector competence or vector survival may eventually also be applicable in biological control.

Effective vaccines for equine use are available for EEE, WEE, and VEE. Many equine populations in the USA and in tropical America, however, remain unvaccinated. In the case of EEE and WEE, vaccination of equine "dead-end" hosts does not preclude human infections, and widespread immunization eliminates the sentinel value of equine disease (as illustrated in Massachusetts in 1974, see above). Immunization of equines against VEE is a limited component of public and veterinary health programmes in a number of countries. Both live attenuated and inactivated vaccines are used. Records of vaccine production and administration by country may be found in the publication *Vigilancia Epidemiologica* of the Pan American Zoonosis Center (Ramos Mejía, Argentina).

Vaccines for the protection of man against the arboviral encephalitides in the Americas are still experimental. Live, attenuated VEE (TC-83) vaccine and inactivated EEE and WEE vaccines are used to protect laboratory and field workers. A promising

inactivated TC-83 vaccine has been developed and is being tested. A killed mouse-brain vaccine against Rocio virus has been prepared in Brazil and tested in human volunteers. Concerning SLE virus, basic research is under way on aspects of strain variation, virulence, genetics, and antigen structure. These investigations are important preliminary steps to the possible development of a vaccine, but the applicability of an SLE vaccine in human populations is controversial.

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## RÉSUMÉ

### Encéphalites transmises par les arthropodes dans les Amériques

Les encéphalites transmises par les arthropodes sont une cause importante de morbidité humaine et équine dans les Amériques. Les 7 virus responsables, dont les 6 principaux sont transmis par des moustiques, sont à l'origine d'épidémies ou d'endémies, à l'exception du virus de l'encéphalite de Californie, associé à une infection de caractère endémique. Les trois encéphalites équines causent une morbidité et une mortalité au moins dix fois plus forte chez le cheval que chez l'homme lors des épidémies et ce tableau épidémiologique est propre aux Amériques. Les cas humains d'étiologie connue notifiés aux Etats-Unis d'Amérique entre 1955 et 1978 se montent à 6970, mais ils ne représentent que 25 à 50 % des cas (tableau 1). Au cours des cinq dernières années, les épidémies d'encéphalite de Saint-Louis et d'encéphalite équine de l'Ouest ont été les plus fréquentes. L'incidence chez les chevaux, moins bien connue, semble peu varier d'une année à l'autre et les activités de surveillance devraient permettre d'en préciser l'étiologie.

La plus grave des infections en cause, tant par ses manifestations cliniques que par son incidence chez l'homme, est l'encéphalite de Saint-Louis (SLE), due à un virus largement présent de l'Argentine au Canada et transmis principalement par deux moustiques: *Culex pipiens pipiens* — très répandu dans l'environnement urbain et suburbain du centre des Etats-Unis — et *C. nigripalpus,* en Floride, qui sont à eux deux responsables de 75 % des cas. Parmi les épidémies récentes (1974 à 1977), la plus étendue s'est produite en 1975 dans le bassin Ohio-Mississipi (1815 cas). Les oiseaux, qui constituent le principal hôte vertébré intermédiaire, sont utilisés comme « sentinelles » pour la surveillance épidémiologique. Les mécanismes de survie du virus pendant l'hiver ne sont pas encore connus et c'est sur ce point qu'ont été axées les recherches récentes.

L'encéphalite équine du Venezuela (VEE) est la principale des encéphalites frappant les équidés. Les divers sérotypes du virus responsable des épizooties sont répandus dans le nord de l'Amérique du Sud (Colombie, Guyane, Equateur et Venezuela). Une forte poussée épizootique s'est prolongée de 1969 à 1972, et elle a causé un nombre élevé de cas mortels chez les équidés au Texas en 1971. Les recherches en cours portent sur

l'origine des épizooties, le rôle des vertébrés autres que les équidés dans le cycle de transmission, et les relations virus/vecteur pour les sous-types enzootiques en Amérique centrale et du Sud. *C.* (*Melanoconion*) *aikenii* et *C.* (*M.*) *Opisthopus,* vecteurs de ces sous-types, font l'objet d'études écologiques.

L'encéphalite équine de l'Est (EEE), due à un alphavirus, frappe les équidés et l'homme, notamment les enfants chez qui elle est souvent fatale. Aux Etats-Unis, son incidence est relativement faible et dispersée, mais assez constante dans le temps. Par contre, le virus est à l'origine d'épizooties en Amérique du Sud, où sa distribution est assez semblable à celle du virus de l'encéphalite équine du Venezuela, mais les cas humains y sont rares. Le sérotype nord-américain du virus a aussi provoqué des épizooties aux Caraïbes, où il peut être transmis par des oiseaux migrateurs et où l'on constate parfois des poussées mixtes des divers types d'encéphalite équine. Une épidémie d'EEE s'est produite en 1973 dans le Massachusetts et le New-Hampshire, causant la mort de 122 chevaux et, dans le Massachusetts, 2 cas humains non mortels. En 1974 et 1975, par contre, 4 cas humains mortels ont été enregistrés dans cet Etat, les chevaux ayant été protégés avec succès grâce à une campagne de vaccination exécutée en 1973. Au Venezuela, 112 cas ont été signalés chez les équidés en 1976, dont 60 mortels. La même année, une poussée s'est produite dans le nord de l'Etat de New York, dont le vecteur enzootique *Culiseta melanura* semble avoir été responsable. En 1978, les cas ont été plus nombreux que d'habitude en Floride (121 chez les équidés et 5 chez l'homme) et des isolements de virus ont pu être opérés chez le même vecteur. Le sérotype nord-américain a aussi été isolé la même année lors d'une épizootie équine survenue en République dominicaine, causant 123 cas mortels, et l'on soupçonne *C. nigripalpus* d'en avoir été le vecteur. Peu de progrès récents ont été signalés dans les recherches sur l'épidémiologie et l'écologie du vecteur.

L'encéphalite équine de l'Ouest (WEE) est une infection aiguë chez les chevaux et l'homme. On a signalé 947 cas humains aux Etats-Unis depuis 1955, dont 186 ces 5 dernières années, généralement limités aux Etats de l'Ouest (Dakota du Nord et du Sud, Minnesota) où le vecteur responsable est *C. tarsalis.* Dans l'Est des Etats-Unis, le virus est sporadiquement transmis par *Culiseta melanura.* Un Etat voisin au Canada (Manitoba) a été également frappé. Le virus a aussi été isolé dans l'Est de l'Amérique du Sud, où les poussées sont généralement d'étiologie mixte. L'Amérique centrale semble indemne. Les épreuves sérologiques ont révélé des différences antigéniques marquées entre les virus WEE transmis par les deux vecteurs. La capacité vectorielle de *C. tarsalis* fait actuellement l'objet d'études approfondies, qui pourraient déboucher sur l'emploi de souches réfractaires pour la lutte biologique.

L'encéphalite à virus Rocio qui, comme l'encéphalite de Saint-Louis, frappe l'homme, n'est connue que depuis 1975, où une épidémie a été enregistrée au Brésil (région côtière de São Paulo). En 1976, l'épidémie a progressé vers le sud. Le total des cas a été de 825.

L'encéphalite de Californie (CE) est due principalement au virus La Crosse, bien connu depuis les années soixante comme agent pathogène humain important (1035 cas de 1963 à 1978). L'infection revêt un caractère endémique, les enfants dans le Centre-Nord des Etats-Unis étant les plus souvent frappés. L'incidence est relativement faible quoiqu'elle ait été particulièrement élevée en 1975 et 1978. Le vecteur est *Aedes triseriatus,* et la transmission transovarienne du virus chez le moustique a été établie. On estime à 4 ans au moins la persistance virale ainsi assurée, indépendamment du cycle moustique/vertébré.

Les chiffres de morbidité et de mortalité cités montrent que, pour l'ensemble des encéphalites arbovirales, les mesures de prévention et de lutte n'ont que peu progressé en dépit des résultats obtenus par la recherche fondamentale. Dans la lutte contre les vecteurs, des difficultés financières et écologiques s'ajoutent au phénomène de résistance, et les populations de vecteurs tendent à s'accroître du fait de la modification de l'environnement par l'homme — notamment de l'irrigation et du développement urbain. On peut cependant prévoir les poussées en surveillant les moustiques et les oiseaux et prendre des mesures antivectorielles en cas d'urgence, au moyen de pulvérisations sous volume ultra-faible. Enfin, bien que des vaccins soient disponibles pour les 3 types d'encéphalite équine, de nombreuses populations équines ne sont pas vaccinées. Lorsqu'elles le sont, d'ailleurs, l'infection humaine n'est pas pour autant écartée et les chevaux ne peuvent plus servir de sentinelles.