Epidemiological features of and public health response to a St. Louis encephalitis epidemic in Florida, 1990–1

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SUMMARY

A St. Louis encephalitis (SLE) epidemic in Florida during 25 weeks in 1990–1, resulted in 222 laboratory-diagnosed cases, an attack rate in the 28 affected counties of 2·25/100000. Disease risk rose with advanced age, to 17·14/100000 in persons over 80 years, and all 14 fatal cases were in persons over 55 years (median, 70 years). Community serosurveys in Indian River County, the epicenter of the outbreak (attack rate 21/100000), showed acute asymptomatic infections in 3·6% of the persons surveyed, with higher rates in persons with outdoor occupational exposure (7·4%) and in clients of a shelter for the indigent (13·3%). A matched case-control study found that evening outdoor exposure for more than 2 h was associated with an increased risk for acquiring illness (odds ratio [OR] 4·33, 95% CI 1·23–15·21) while a number of recommended personal protective measures were protective. Four SLE patients were dually infected with Highlands J virus, the first reported cases of acute infection with this alphavirus. The case-control study provided the first evidence that a public education campaign to reduce exposure had a protective effect against acquiring the disease.

INTRODUCTION

St. Louis encephalitis (SLE) is a mosquito-borne flavivivirus infection that was first recognized when a virulent outbreak of 1095 cases occurred in St. Louis in 1933 [1]. In the United States, SLE is transmitted by various species of *Culex* mosquitoes to birds, which function as viral amplifying hosts, and during years when conditions favour a higher intensity of viral transmission, also to humans, who are dead-end hosts [2–4]. The principal vector in Florida, *Culex nigripalpus*, is widely distributed in rural and suburban areas where larval stages breed in ditches and grassy pools and adults shelter in densely vegetated locations. Adults emerge into open areas to feed, principally on

birds early in the year, and more opportunistically on mammals as well, in the summer and autumn.

In the eastern United States, SLE occurs in sporadic, usually geographically localized, outbreaks. In Florida, outbreaks have occurred in 1958 (Miami; 4 cases); 1959 (Tampa Bay area; 68 cases); 1961 (Tampa Bay area; 25 cases); 1962 (Tampa Bay area; 231 confirmed and presumptive cases); 1977 (central-south Florida; 110 cases); and 1980 (Fort Walton Beach; 5 cases) [5–10]. During interepidemic years, the virus is transmitted with considerable intensity in the enzootic cycle, reflected in seroconversion rates exceeding 50% in sentinel chickens, with little spillover to humans [11]. In most years, 0–4 sporadic cases in humans are reported in the state.

During the summer of 1990 and extending into the winter of the following year, a widespread SLE

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outbreak in central Florida, second in size only to the 1962 epidemic, led to 222 cases. Based on what is known about the behaviour of *Culex nigripalpus* mosquitoes, in the 1990–1 epidemic, a major public health intervention was launched that advised residents in the affected areas to limit their outdoor activities during the early morning and evening hours when vector mosquitoes are most active. Although this recommendation has been promulgated routinely during previous outbreaks, its effectiveness in preventing cases of disease has never been evaluated. We report here epidemiological characteristics of the outbreak and factors emerging from a case-control study, that were associated with protection and risk for acquiring the illness.

METHODS

Descriptive epidemiology

Case finding was accomplished through an active surveillance system that was instituted by the Florida Department of Health and Rehabilitative Services (DHRS) in July of 1990, shortly after the first few suspected SLE cases were reported. Hospital infection control nurses actively sought suspected cases among daily admissions and notified county health officers. They in turn reported to the state an updated weekly line list, by telephone or electronically, of previously reported as well as newly suspected cases. Suspected cases were also reported directly by clinical laboratories and by hospitals and health care providers. County public health units followed up all suspected cases to obtain additional clinical and epidemiological data, and acute and convalescent phase serum samples and cerebrospinal fluid (CSF) samples for laboratory diagnosis.

Laboratory methods

Laboratory diagnosis was sought by various serological methods in a commercial reference laboratory (according to the convenience of the attending physician), the Florida State DHRS public health laboratory and at the Centers for Disease Control and Prevention (CDC), Ft. Collins, CO. In a small number of cases, a commercially available indirect immunofluorescent antibody kit was used to confirm cases directly (Microbiology Reference Laboratory). In the majority of cases, however, specimens were sent to the Florida State DHRS laboratory where hemagglutin-

ation inhibition (HI) and IgM ELISA determinations were performed, and when sufficient volume of specimen remained (in 512 cases), to the CDC for confirmation of IgM ELISA determinations [12].

As directed by the manufacturer, IFA antibodies were measured by reacting serum samples in twofold dilutions, beginning at 1 in 16, against Vero cells infected with SLE, western equine encephalitis (WEE), eastern equine encephalitis (EEE), or La-Crosse viruses. For HI determinations, sera were acetone extracted and tested in twofold dilutions beginning at 1 in 10 against SLE and EEE viral antigens. At CDC, serum samples (diluted 1 in 100) and CSF (undiluted) were tested in IgM capture assays against SLE, Everglades (Venezuelan equine encephalitis IV virus), Highlands J virus (a WEE related alphavirus) and EEE virus. After serum or CSF was added to wells sensitized with anti μ chain antibodies, crude sucrose-acetone extracted infected mouse brain viral or control antigens were added, and if bound by viral-specific IgM, the antigen was detected with horseradish peroxidase-labelled flaviviral or alphaviral reactive monoclonal antibodies. Samples with absorbance ratios twofold or higher to the viral antigen over the control antigen were considered qualitatively positive.

Case definition

Cases were assigned to one of the following categories based upon a combination of clinical and laboratory criteria. The clinical element of the definition required the acute onset of a febrile illness with fever and headache or other central nervous system abnormality. Suspected cases were patients in whom there was a clinical suspicion but in whom laboratory confirmation was incomplete and presumptive cases were those meeting the clinical definition and who had a single hemagglutination inhibition titre (HI) of greater than or equal to 40, or a single IFA titre of greater than or equal to 64 and confirmed cases if a fourfold or greater rise or fall between acute and convalescent antibody titres with one titre greater than or equal to 40 (HI) or 64 (IFA), or a positive serum or cerebrospinal fluid (CSF) IgM antibody test was found. Non-cases had two negative serological tests at least 14 days apart, or one negative test and another diagnosis. Information obtained for each case included demographics, date of onset of symptoms, laboratory information, and a brief clinical description. Counties were asked to categorize cases into

those with encephalitis, defined by the presence of CSF pleocytosis and one or more of: mental status change, gait disturbance, seizure or focal neurological finding; meningitis, defined as the presence of CSF pleocytosis without signs or symptoms of encephalitis; or viral/other illness, which were either patients with non-specific symptoms of an acute flu-like illness without CSF pleocytosis, or a viral illness not evaluated by lumbar puncture.

Medical records were obtained for 161 of the confirmed and presumptive cases, and those data were entered into a database that allowed patients to be categorized by case type and clinical category. Data were analysed by univariate analysis and disease rates were calculated using 1990 census county and state-specific population data.

Case-control study

Confirmed or presumptive cases from five of the most significantly affected counties were randomly selected for telephone interviews. Selected cases were considered candidates for interview if they had not moved out of state, spoke English fluently, and consented to participate. Controls were individually matched to each case by age (± 5 years), sex, county of residence, and 3-digit telephone prefix. Control subjects were identified using randomly selected phone numbers from the residential telephone book that contained the listings for the case patient's 3-digit prefix. Interviews were conducted during January 1991. The interviews largely focused on the respondent's amount of outdoor daytime and evening activities, and on each respondent's knowledge of and use of protective measures. Each case-control pair was interviewed by telephone by the same individual. Matched case-control analysis was done using Epi-info version 5.

Community serosurveys

Three serosurveys were conducted in Indian River County in the last week of October to assess the incidence of infection in areas of the county and to evaluate risk factors for acquiring infection during this epidemic. The county had an estimated population of 90000, concentrated primarily along the Atlantic coast and on a barrier island. To the West, are large expanses of citrus groves, which serve as excellent breeding sites for *Culex nigripalpus*. Central

Vero Beach and the Sebastian Highlands were chosen as sites for residence-based sampling. The populations of both were predominantly middle class with a high proportion of retired persons. We enrolled households by telephone, using a cluster sampling method in which starting households for each cluster were selected at random from a reverse telephone directory. Residents of adjacent houses on the same street were contacted until at least seven participants were enrolled in the cluster. Repeated attempts were made to contact households where no one answered the telephone; these households were counted in the denominator when calculating completion rates. At home visits a brief questionnaire was administered for each consenting person and a sample of venous blood was collected.

Because our sampling strategy appeared to favour enrolment of older individuals whose outdoor exposure and opportunities for acquiring infection might have been limited, we obtained additional samples and questionnaire data from volunteers in occupational and residential groups considered to be at high risk of exposure. These groups included citrus grove workers, employees of the county Mosquito Control District and the Florida Medical Entomology Laboratory, county environmental health employees, employees of the Sebastian Police Department, residents of a mobile home park in the western part of the county and lower socioeconomic status clients of a shelter in the Gifford area. SLE infections in respondents were determined serologically by IgM capture ELISA.

RESULTS

Descriptive epidemiology

Between 28 July 1990, and 12 January 1991, 1142 suspect SLE cases were reported and investigated; of these, 338 were ruled out by laboratory tests, 50 were diagnosed as presumptive cases, and 172 were confirmed cases. Lack of adequate specimens and clinical information did not allow classification of the remaining suspect cases. The 222 laboratory-diagnosed cases yielded an attack rate for Florida for the epidemic period of 1·72 confirmed and presumptive cases per 100000 population. Using only the combined populations of the 28 affected counties as the population denominator, the attack rate was 2·25 per 100000. Indian River County reported the highest attack rate of 21 cases per 100000 and, at the other
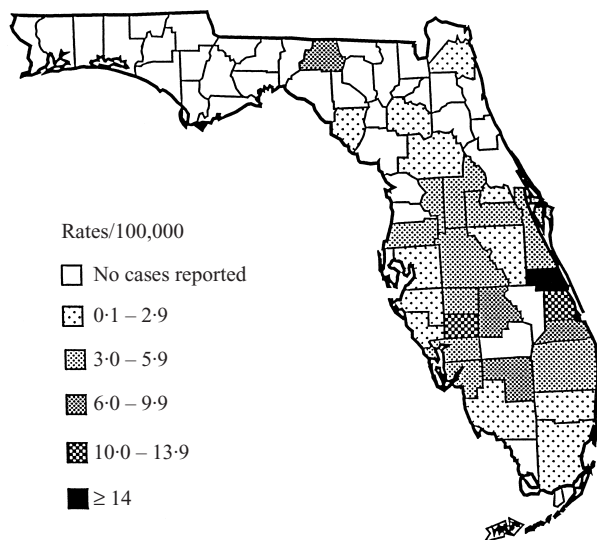
Fig. 1. St. Louis encephalitis county specific attack rates, 1990–1, per 100000.
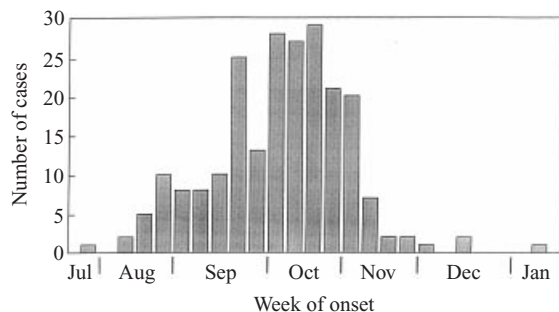

Fig. 2. St. Louis encephalitis cases, Florida, 1990–1, by week of onset.

extreme, five counties reported only one case each (Fig. 1).

The epidemic curve of confirmed and presumptive cases by week of onset shows that new cases occurred over a 25 week period, extending from midsummer to midwinter (Fig. 2). The median age for confirmed and presumptive cases was 54 years (range 5–91 years). Age-specific attack rates for the affected counties rose from 0·49 per 100000 for the 0–19 year age group to 17·14 per 100000 for persons over age 80 (Table 1). The attack rates by gender and race are shown in Table 1.

Of the 222 laboratory-diagnosed cases, 82 had encephalitis, 43 had meningitis, and 97 had symptoms of a viral illness. Fourteen patients died, a case fatality rate of 6·3% and a mortality rate in the affected counties of 0·14 per 100000. All deaths occurred in patients over age 55 years (median age, 70 years).

No cases of EEE or Everglades viral infection were diagnosed but four patients with presumptive SLE

Table 1. *St. Louis encephalitis attack rates for the 28 affected counties*, Florida, 1990–1 (222 *laboratory confirmed and presumptive cases*)

Demographic group	Rate per 100000
Total population	2·25
Gender	
Male	2·50
Female	2·02
Race	
White	2·29
Non-white	1·37
Age group (years)	
0–19	0·49
20–39	2·21
40–59	3·16
60–79	3·50
80+	17·14

also exhibited elevated IgM antibodies to Highlands J virus in paired serum samples and were considered possible cases of dual infection (Table 2).

Case control study

Of 75 case-patients selected for interview, 19 were not enrolled because a working phone number could not be found, because they had moved out of state, were in prison or jail, or did not speak English. Ten others refused, or were never matched with an appropriate control. Of the 46 pairs suitable for analysis, 24 were female and 22 were male. Racial and ethnic group of the 46 case patients was 37 white, non-Hispanic, 6 African-American and 3 Hispanic. Of the 46 matched controls, 2 were African-American and 3 were Hispanic.

In the matched analysis, several behaviours and changes in behaviour were associated with a lower risk of acquiring SLE (Table 3). Awareness of the health recommendations that had been publicised to prevent infection was strongly associated with a reduced risk of acquiring illness, with an eightfold lower risk among persons who professed knowledge of the recommendations. Beyond awareness, the purposeful reduction of outdoor activity during the evening was associated with a fourfold lower disease risk. On the other hand, outdoor activity of greater than 2 h during the evening was associated with a fourfold greater risk of acquiring illness, although outdoor employment during the evening was not associated with an elevated risk. Having an air

Table 2. *St. Louis encephalitis and Highlands J virus IgM antibodies in acute and convalescent serum samples of four encephalitis cases, Florida, 1990*

| Onset date of symptoms | Sample date | IgM ELISA absorbance ratios* | |
		Highlands J virus	St. Louis encephalitis virus
23/8/90	27/8/90	2·25	12·7
	9/9/90	3·61	12·0
5/9/90	8/9/90	6·07	10·4
	21/9/90	5·64	11·8
1/9/90	17/9/90	7·22	3·25
	9/24/90	3·02	2·91
Unknown	6/11/90	5·70	7·79
	23/11/90	4·24	7·15

* Absorbance ratios $\geqslant 2\cdot0$ are positive.

Table 3. *Results of matched case-control analysis for selected variables: St. Louis encephalitis investigation, Florida 1990–1*

Variable	Matched odds ratio	95% confidence interval	χ^2	P value
Air conditioner in home	0·20	0·04–0·91	4·08	·04
Wore repellant in evenings	0·60	0·26–1·37	1·04	·307
Wore long trousers in evenings	0·35	0·14–0·90	4·35	0·37
Wore long sleeves in evening hours	0·36	0·13–0·99	3·37	0·66
Employed outside during evening hours	0·40	0·08–2·06	0·57	·450
Outside evening activity longer than 2 h	4·33	1·23–15·21	5·06	·024
Purposely limited evening activities	0·26	0·10–0·70	7·04	·008
Aware of public health recommendations	0·13	0·03–3·58	8·47	·0036
Screens on windows in house	0·33	0·03–3·20	0·25	0·60
Watered lawn in evening	1·11	0·45–2·73	0	1·00

conditioner and using it sometimes or usually, wearing shirts with long sleeves in the evening, and wearing long trousers in the evening, were all protective and were associated with an odds-ratio of less than one. Using repellant in the evening was not significantly related to disease risk.

Community serosurveys

A total of 505 serum specimens with accompanying questionnaire data were collected, 308 from households in the two sampled residential areas. In the Sebastian Highlands area, 150 specimens were obtained from individuals in 83 households, representing 8·5% of its population (according to 1990 census estimates) and from central Vero Beach, 158 specimens were obtained from 97 households, representing 5·2% of the 1990 estimate. Household questionnaire completion rates were 60% (80 of 133 households

contacted) for Sebastian Highlands and 56% (89/160) for central Vero Beach. Volunteer samples were obtained from the various groups perceived at high risk as shown in Table 4.

The point prevalence of SLE virus-specific IgM antibodies, indicating aysmptomatic recent infection, was 2·1% in the residents of the three neighbourhoods surveyed and 7·4% among the occupational groups with outdoor exposure perceived to be at higher risk, and 13·3% among lower socioeconomic status persons attending a shelter (Table 3). As a group, respondents with an air-conditioned residence had a significantly lower infection rate (2·7%), compared with persons living without air-conditioning (10·7%) ($\chi^2 = 9\cdot163$, $P < 0\cdot002$). Only 5% of persons in the middle-class residential communities surveyed lived in non-airconditioned residences compared with 64% of persons from the lower socioeconomic class area. The low seroprevalence rate did not permit further analysis

Table 4. *St. Louis encephalitis (SLE) virus point seroprevalence by study group, Indian River County, Florida, 1990*

Study group	SLE virus IgM antibody prevalence
Residential neighbourhoods*†	
Vero Beach	4/158 (2·5%)
Sebastian Highlands	3/150 (2·0%)
Heron Cay mobile home park	0/29
Occupational Groups*	
Environmental health	1/37 (2·7%)
Sebastian Police Department	0/10
Mosquito control workers	0/11
Entomology laboratory personnel	3/34 (8·8%)
Orchard workers	3/42 (7·1%)
Low socioeconomic status clients of shelter†	4/30 (13·3%)
Unknown	0/4
Total	18/505 (3·6%)

* $\chi^2_{(1)} = 6·7$, $P < 0·01$.
† $\chi^2_{(1)} = 12$, $P < 0·001$.

of infection risk within subcategories, or for behaviours such as outdoor activity at dusk, heeding public health warnings to avoid mosquito exposure, or characteristics of primary residences, such as presence of shrubs and trees. There were no significant differences in risk of infection by age or sex. No racial differences in risk could be differentiated when accessibility to air-conditioned residences was taken into consideration; only 25% of blacks had access to an air-conditioned residence compared to 93% of whites.

DISCUSSION

Among the previous six reported SLE outbreaks in Florida, the 1990–1 epidemic was most similar to the one that occurred in 1977 that also diffusely involved an extensive area of the central and southern peninsula [9]. In terms of numbers of cases, geographic extent and duration, however, the 1990–1 outbreak was unique, and required extensive, coordinated surveillance and control efforts. Although 222 cases had a laboratory diagnosis, the actual extent of the epidemic was undoubtedly greater, because an additional 562 patients who were clinically suspected of having SLE, but in whom information or adequate specimens were lacking, could not be confirmed as cases.

The community surveys in Indian River County that found an overall 3·6% infection rate confirm a high rate of case ascertainment in that county. Extrapolating from the well established asymptomatic infection to symptomatic case ratio of approximately 300:1 for SLE, an attack rate of 12/100000 in the county was expected, while the reported incidence was 21/100000 [2, 13]. The discrepancy is more likely a result of a falsely low seroprevalence rate due to biases in the population groups sampled and the decay of IgM antibodies in persons who were infected earlier in the outbreak. Since the serosurvey was completed at the end of October, an unknown proportion of persons asymptomatically infected in early and mid-summer and whose IgM antibody response had declined by October, would have been classified as seronegative in the survey [14].

Suggestions that SLE might emerge in a statewide epidemic in 1990 were apparent as early as the autumn of 1989 from surveillance of sentinel chickens, which showed record levels of seroconversions between October and December. Local patterns of increased rainfall that led to unusually abundant vector populations were recorded in Indian River County and undoubtedly contributed locally to increased spillover of viral transmission to humans [15]. Following heavy rains in May and June 1990, mosquito surveillance disclosed unusually large populations of *Culex nigripalpus* mosquitoes, not usually seen before the autumn, by the end of June and, on 16 July, the earliest seroconversions in sentinel chickens in the 12 year history of the surveillance programme were detected. Under other permissive conditions, the early onset of viral transmission in the enzootic cycle provided an extended opportunity for viral load in the natural cycle to build up and overflow to humans.

On the basis of these indications of unusually intense SLE viral transmission and before any cases had emerged, the medical community and public were warned of an impending epidemic and advice was issued to restrict outdoor activity at dusk and dawn. After several clinically compatible cases were hospitalized in mid-August, a formal encephalitis alert was issued, public health warnings to avoid evening mosquito exposure were intensified and aerial spraying and larvicide applications were initiated. Public health warnings recommended several specific alterations in behaviour to lower the risk of exposure to vector mosquitoes (staying in air-conditioned buildings, limiting outdoor evening activities, wearing long trousers and long sleeved shirts when outdoors, and using mosquito repellant). To further reduce the risk among the public, numerous outdoor evening func-

tions were either cancelled or rescheduled to daylight hours. Broadcasts of public health warnings as part of the extensive media coverage of the epidemic helped to reinforce the recommended protective behaviour.

Although similar public education and warning announcements are broadcast routinely during SLE and other mosquito-borne disease outbreaks, their effectiveness in reducing the risk of disease has never been measured. After a SLE outbreak in Pine Bluff, Arkansas, a serosurvey showed that uninfected persons were more likely to have known about recommended mosquito avoidance behaviours than asymptomatically infected persons, although the actual protective effect of this knowledge could not be inferred, because infections had already occurred in the population when the survey was undertaken [16]. Results from this case-control study extend these observations by showing that beyond awareness and knowledge of the public education message, persons who initiated purposeful behavioural changes to reduce outdoor activity were fourfold less likely to acquire the disease.

Several limitations to the studies discussed above deserve mention. The case-control study, although matched on some variables, may suffer from bias related to the use of telephones as the method of contact, the requirement that the respondents speak English and the need for respondents to have a fixed residence. The fact that we were able to locate and include as cases only 61 % of the cases selected may reflect these possible biases. The serosurvey data included some data from randomly selected samples from certain neighbourhoods in Indian River County. Some of the data are from specific occupational groups thought to possibly be at high risk. Therefore the overall rate of seropositivity of 3·8 % does not necessarily represent that of the community as a whole.

The highest infection rates in the serosurvey were among persons who attended a shelter for the homeless and impoverished in Gifford, a low socio-economic area of Indian River County. High attack rates in low socioeconomic neighbourhoods has been a frequent feature of SLE outbreaks, because characteristics of those areas, such as old houses with open foundations, provide mosquito breeding or resting sites but, homelessness and absence of air-conditioned or adequately screened residences, also have been noted as common factors [2, 3, 13, 16–18]. In recent *Culex quinquefasciatus*-borne outbreaks in Dallas and New Orleans, 9 of 36 cases were homeless, a proportion considerably at odds with the expected rate in the general population, although, in one of those observations, homelessness and HIV infection were confounding variables [19, 20].

While we believe that the risk of acquiring SLE was modified by a reduction of outdoor activities in the evening, this recommended action presumes that retreat to a location, usually a residence, protected against mosquitoes is possible. Consideration should be given to combining public warnings to avoid outdoor activity with assistance to provide shelters for persons without access to air-conditioned or screened residences. Just as heated or air-conditioned shelters are made available to the homeless during periods of extreme cold or heat, public authorities should consider distributing door and window screens to low socioeconomic areas and opening shelters to the homeless during SLE outbreaks [17, 18].

Although the 1990–1 SLE epidemic produced a near record number of 222 laboratory diagnosed cases, a total of 1142 suspected cases were investigated and only 338 patients were ruled out, meaning that SLE accounted for only 40 % (222 of 560 cases with adequate laboratory samples) of the evaluable encephalitis cases in that interval. We tested 521 suspected cases for IgM antibodies to Everglades and Highlands J (HJ) viruses, both arboviruses that were isolated initially in Florida, the former from the Great Everglades swamp and the latter in Highland County, Florida [21, 22]. Everglades virus, a subtype of Venezuelan equine encephalitis virus, which has previously been implicated in only three human encephalitis cases in the USA, all in elderly persons, is transmitted by swamp-dwelling mosquitoes to cotton rats [21]. As a 'place' disease, infections usually are acquired in the relatively remote locations where the viral cycle is maintained. The absence of any cases among the 521 patients evaluated in 1990–1 was therefore not unexpected, because patient referrals came mainly from central counties, north of the virus's known range. The four patients with HJ IgM antibodies are the first reported cases of acute human infection with this alphavirus. The patients exhibited changes in virus-specific IgM reflecting recent infections, while the absence of similar rises to Everglades and EEE viral antigens ruled out a non-specific IgM reaction. However, parallel reactions to SLE virus suggest that the concurrent alphaviral infections were incidental. HJ virus is closely related to western equine encephalitis virus and has been implicated in encephalitis cases in Florida horses, but never in

humans [22]. A role for the virus in human central nervous system infection is possible, but no patients infected independently with the virus were found among the 512 patients studied.

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