Epidemic Venezuelan Equine Encephalitis in La Guajira, Colombia, 1995

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In 1995, the first Venezuelan equine encephalitis (VEE) outbreak in Colombia in 22 years caused an estimated 75,000 human cases, 3000 with neurologic complications and 300 fatal, in La Guajira State. Of the state's estimated 50,000 equines, 8% may have died. An epizootic IC virus, probably introduced from Venezuela, was rapidly amplified among unvaccinated equines. Record high rainfall, producing high densities of vector *Aedes taeniorhynchus,* led to extensive epidemic transmission (30% attack rate) in the four affected municipalities. Native Wayuu Indians, constituting 24% of the state's population, were at increased risk of infection (risk ratio, 3.3; 95% confidence interval, 2.2–5.3). Epidemiologic studies found no evidence of human-to-human transmission. A higher-than-expected number of abortions during the outbreak confirmed a previously suspected abortifacient role of VEE infection. Pesticide applications and a mass equine vaccination program contributed to preventing the outbreak's spread south of La Guajira.

Venezuelan equine encephalitis (VEE), an arbovirus disease that periodically emerges in combined epidemics and epizootics in tropical America, last occurred in an extensive outbreak in 1973 [1, 2]. In April 1995, an outbreak due to VEE epizootic subtype IC virus erupted in Falcon State, Venezuela [3, 4]. By mid-August, native Wayuu Indians reported deaths among their unvaccinated donkeys, as tribes made their annual journey from Zulia State, Venezuela, to Colombia's Caribbean coast to collect salt (figure 1). Heavy rains from May to late October, the heaviest precipitation recorded in La Guajira in the previous 18 years, delayed their arrival in Manaure until late August. On 8 September 1995, an outbreak of acute febrile illness was reported to the Ministry of Health (MOH) of Colombia by La Guajira Health Administration (DASALUD). This report describes the public health response, epidemiologic investigation, and field studies to measure secondary transmission and clinical effects of VEE in pregnancy.

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Materials and Methods

Preliminary investigations and surveillance. Initial suspicions that the outbreak was dengue were disproved when preliminary surveys of cases found no hemorrhage or rash. Reports of antecedent equine deaths in affected villages and isolations of VEE virus from early clinical specimens confirmed the etiology as VEE. The MOH declared a national emergency and DASALUD established active surveillance in the 14 municipalities of La Guajira to identify daily emergency room and hospital visits for acute febrile illness, cases meeting a preestablished case definition, and equine deaths.

Hospitalized patients with neurologic or obstetric complications. Records of patients hospitalized in Riohacha, Manaure, Uribia, and Maicao municipalities between 1 September and 10 October 1995 and discharged with a VEE-compatible diagnosis (dengue, virosis, encephalitis, viral infection, or febrile seizures) were reviewed. A team of neurologists examined selected patients with neurologic complications, including convulsions, behavioral changes, and disturbances of consciousness. To confirm the suspected abortifacient potential of VEE virus, records of spontaneous abortions at the Riohacha hospital from 1993 to September 1995 were reviewed.

Epidemiologic field investigations. Between 25 September to 3 October 1995, we conducted clinical-epidemiologic surveys of randomly selected households in urban limits of Manaure, Riohacha, Maicao, and Uribia using a cluster sample design [5]. Smaller towns and scattered settlements along the coastline (El Pajaro, Mayapo, Musichi, Camarones, Pelechua, Montañita, and Dibulla) were investigated to assess attack rates and to trigger control activi-

Figure 1. Map of La Guajira state, Colombia, showing locations of human and equine VEE cases (□) and attack rates in human populations by municipality, 1995. Height of bars indicates attack rate shown as %. ◆ = locations of reported equine deaths.
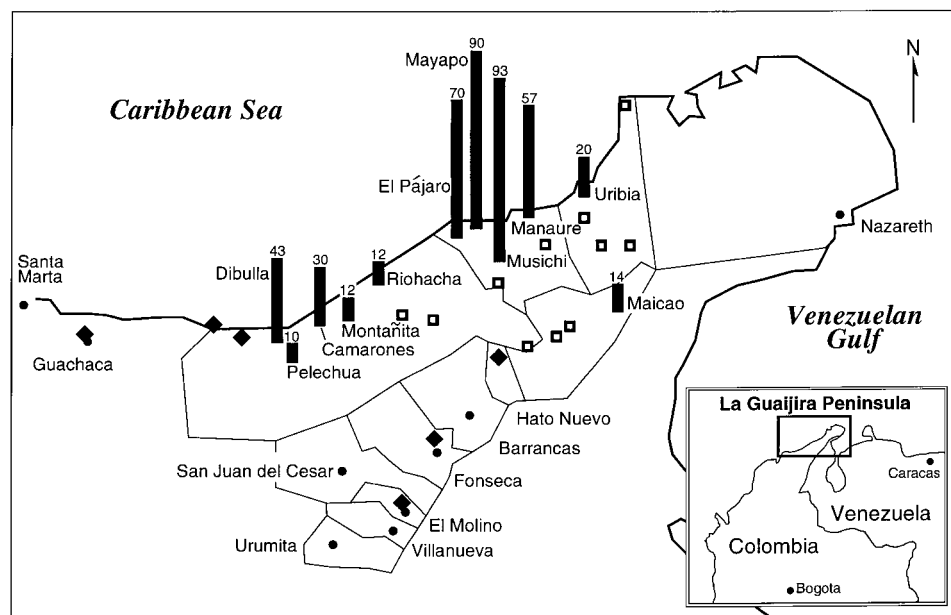
ties (figure 1). Households in Maicao, Riohacha, and Uribia that had >1 case were studied to determine the extent of secondary transmission. A secondary case was defined as a person having acute febrile illness beginning 1–5 days after onset in the first case(s) in the household. Primary cases occurring within 5 days of the interview and households with a single resident were excluded.

A serosurvey in the four municipalities (total population, ~300,000) was conducted during 16–26 November using the most current list of towns and villages as a sampling frame to select 30 clusters with probability proportional to size. Seven persons were selected in each cluster, and blood samples and relevant clinical and epidemiologic information were collected, including onset date of a ''peste loca'' (mad plague)–like illness, ownership of donkeys, mules, or horses, the animals' vaccination status, and whether any animals had died. Blood samples were collected from unvaccinated donkeys.

Virologic investigations. Serum samples from acute febrile patients were processed for virus isolation at the Colombian National Institute of Health (NIH) Virology Laboratory, and isolates were further characterized at the University of Texas Medical Branch (Galveston) and the Yale Arbovirus Research Unit (New Haven, CT). Serologic tests were done using US Army Medical Research Institute of Infectious Diseases IgM capture and indirect IgG ELISA kits [6].

Entomologic investigations. Entomologic surveys identified epidemic vectors and assessed the effectiveness of control activities. Potential breeding sites were inspected, and adult mosquitoes were captured in the epidemic zone and in selected areas without reported activity. Adult mosquitoes were frozen for virus isolation.

Statistical analysis. Attack rates were calculated as binomial proportions from random sample cluster design estimators. Greenland-Breslow-Robins estimators of relative risk, confidence interval estimates for proportions and rates, and χ^2 tests all were calculated with Epi Info 6 [7].

Results

VEE Surveillance. From 8 September to 10 October 1995, 22,900 outpatients and 1220 hospitalized patients with an illness suspected to be VEE were reported from La Guajira. Onset dates of cases in urban areas of Riohacha, Maicao, and Uribia are displayed in figure 2. The VEE epizootic/epidemic spread through the affected areas at a rate of 5 km/day. In total, 26 VEE-associated human deaths were reported to the MOH.

No confirmed equine cases of VEE were reported outside La Guajira State. Within La Guajira, equine deaths occurred sporadically, except for a cluster of 77 deaths in Manaure. Review of equine vaccination records showed a steady decline in TC-83 vaccine distribution since the mid-1980s. In 1994,
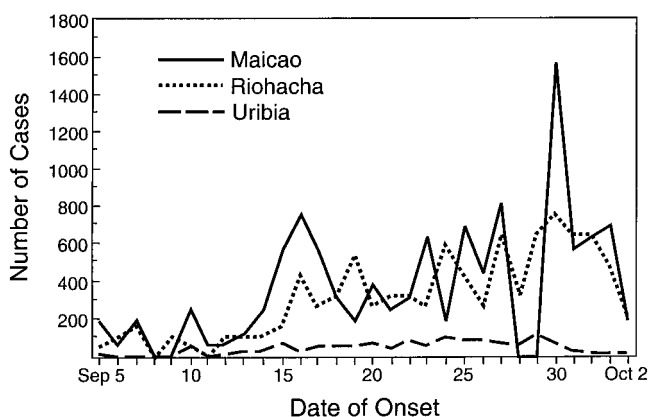

Figure 2. Clinical cases of febrile illness found in household surveys in Maicao, Riohacha, and Uribia, municipalities in La Guajira State, Colombia, 1995.

only 7000 doses were distributed, mostly in the south of La Guajira and to more commercially valuable horses.

Hospitalized cases with neurologic and obstetric complications. Between 25 August and 14 October, 295 patients with VEE-compatible disease were hospitalized. Their residences and illness onset dates were representative of nonhospitalized cases; their median age was 6 years and 56% were female. The proportion of cases with significant neurologic involvement was highest (85%) in children <10 years old; proportions were 1%–2% among adults 20–49 years old and 15% in older adults. The mean length of hospitalization was 3 days; 15 of the patients died (5.1%).

Neurologic examination of 65 patients disclosed an onset of neurologic symptoms 4 days (range, 0–14) after onset of illness. Fever (98%), headache (87% in children >3 years old), and vomiting (63%) were the most common symptoms. Examination disclosed hemiparesis or behavioral abnormalities in 7 patients each (11%); a history of acute convulsions in 62 (95%), of whom 26 had focal seizures; and stupor or coma in 2 (3%). One 7-year-old child had residual hemichorea following ipsilateral motor seizures.

During the outbreak's peak in September 1995, there were 40 spontaneous abortions, compared with a mean of 20/month earlier in 1995 and an average of <18/month in 1994 and 1993. No other month in these 3 years had as many as 40 abortions. Because most of the women lived in rural areas (rancherias) without known addresses, only 10 were located for serologic testing. One had a positive result, a similar proportion as the general population.

Epidemiologic field investigations. Random household clinical surveys of 2749 subjects in urban Manaure, Riohacha, Maicao, and Uribia disclosed attack rates of 13%–57% (14.4% overall; 95% confidence interval [CI], 11.7–17.0) and an estimated 23,000 cases (95% CI, 18,687–27,153). All age groups and both sexes were affected equally. Local outbreaks peaked from mid-September to early October and lasted 6 weeks. In Manaure, as many as 170 new cases a day were recognized at the peak of the epidemic. In El Pajaro, Musichi, Mayapo, Camarones, Montañita, Pelechua, Dibulla, and other smaller towns, attack rates ranged as high as 93% (figure 1). A sine-wave pattern of every-other-day peaks in incident cases was found in every survey (figure 2).

There were 82 households with ≥2 cases, of which 94 were considered primary cases, 50 potential secondary cases, and 76 cases that occurred later. Most of the 126 secondary and later cases occurred within a week after onset of the primary case. There were 992 persons other than those having primary cases in dwellings with >1 person and where at least 1 primary case occurred. Thus, the overall attack rate among household members was 12.7%. The attack rate for the 5-day interval after onset of the primary case was 5%, indicating no significant role for person-to-person transmission.

A total of 382 persons in 57 randomly selected households participated in the cluster serosurvey; 170 persons were sero-positive, for an overall infection rate of 35.9% (95% CI, 22.4–49.4). The clinical case definition used in the cluster serosurvey had a sensitivity of 69% (95% CI, 54–81) and specificity of 64% (95% CI, 54–72). One VEE-associated death was reported in these 57 households, for an estimate of 7 deaths/1000 cases.

Using these rates, the final size of the epidemic was estimated to be 75,000 cases (95% CI, 45,000–105,000), more than three times the number reported from local health centers and hospitals. We estimate a total of 3000 VEE cases with neurologic involvement and 300 VEE-associated deaths by applying a conservative estimate of 5 deaths/1000 cases. Seroprevalence was not biased by age, sex, or urban or rural residence. People with Wayuu (native) surnames, who constitute 24% of the population in La Guajira, had an increased risk of infection (RR, 3.3; 95% CI, 2.2–5.3).

An estimated total of 49,626 equines (95% CI, 1492–97,388) were owned by farmers in the four La Guajira municipalities. No deaths were reported by equine owners in the surveys, yielding an upper 95% limit (Poisson distribution) for proportion of equine deaths of 8% (or 400). Most of the equines (83%) owned by survey respondents were donkeys: 92% of these animals were vaccinated but only 5 (8%) of 60 had been vaccinated before the epidemic's onset. All 10 unvaccinated donkeys and 2 donkeys without owners who participated in the serosurvey were seropositive.

Laboratory results. Seventy VEE virus isolates were recovered from serum samples from 337 acutely ill patients; isolates were identified as VEE strain IC. Limited RNA sequencing showed that this virus was identical to isolates obtained in April from Venezuela and similar to strains that caused the 1963 La Guajira outbreak [8]. IgM testing found an overall seropositivity rate of 45% among acute febrile patients seen in emergency rooms and in persons meeting the case definition of illness in surveys. A strain of VEE IC virus was isolated from 1 of 26 pools of 964 adult female mosquitoes.

Entomologic findings. Larval and adult mosquito densities of several species were elevated. Notably, larval densities of *Aedes taeniorhynchus,* a known VEE vector, were as high as 150,000 larvae/m^2 of surface water in coastal brackish swamps. Inland, high densities of *Culex quinquefasciatus* were found. Although other potential vectors, such as *Deinocerites pseudes* and *Psorophora confinnis,* also were collected, *A. taeniorhynchus* accounted for 77% of the 964 adult female mosquitoes captured for virus isolation. In addition, the highest attack rates occurred in locations where *A. taeniorhynchus* was abundant, implicating this species as the principal epizootic/epidemic vector. *A. taeniorhynchus* was found in its typical breeding sites, especially in coastal marshes of "platanito," a plant of the Aizoacea family *(Sesuvium portulacastrum L.).* Field evaluations indicated that malathion spraying was highly effective in reducing indices of adult mosquitoes. Application of *Bacillus sphaericus* proved to be 99%–100% effective in decreasing larval indices in breeding sites, such as ponds and temporary ground pools, 15 days after the initial application.

Epidemic/epizootic control measures. Beginning 17 September, local public health workers applied pyrethroids and malathion to control adult mosquitoes; because of initial concerns that the outbreak was dengue, community clean-up campaigns and addition of temephos to stored water were initiated to control *Aedes aegypti* breeding sites. Movements of animals within and from La Guajira were restricted by roadblocks. A massive equine vaccination campaign with attenuated TC-83 vaccine was launched in the outbreak area to create a ring of immune equines surrounding the epizootic zone. Vaccination efforts were concentrated in natural corridors to the southeast and southwest of the Sierra Nevada de Santa Marta mountains to prevent the outbreak's spread to Magdalena and Cesar States. No human or equine cases were confirmed south of La Guajira. More than 300,000 doses were distributed nationwide, yielding a 90% vaccination coverage in La Guajira. No further human or equine VEE cases had been reported as of 15 April 1996.

Discussion

In 1995, 60 years after the first recorded VEE outbreak and nearly 25 years after the last major outbreak in South America, the disease reemerged in northern Venezuela and Colombia, the site of numerous combined epizootics and epidemics since the last century [1, 2, 9, 10]. In Colombia, VEE epizootics/epidemics have occurred every 15–20 years, in years with heavy rainfall. In the last decade, equine immunization rates in the native territory had declined, leaving a highly susceptible population of amplifying hosts, especially unimmunized donkeys.

Heavy rains and flooding in the normally arid La Guajira led to a proliferation of *A. taeniorhynchus* and floodwater *P. confinnis* mosquitoes, the principal VEE vectors in previous outbreaks. It is likely that native Wayuu people and their animals, traveling from epidemic areas in Venezuela across the La Guajira peninsula, brought the virus to the Caribbean coast, where it spread southward. Factors underlying the emergence of the epizootic in Venezuela are only partially understood; however, genetic analyses suggest that the epizootic IC strain arose by mutation from sylvatic ID strains maintained in silent rodent-mosquito reservoirs [11–13]. The availability of susceptible equines provided the means for the virus's emergence and amplification. VEE virus is transmitted rapidly among equines and from equines to humans by a variety of arthropod vectors, creating a moving front of transmission measurable in kilometers per day. Epidemic transmission ceases after susceptible amplifying hosts are ''exhausted'' by natural infection or immunization.

Population-based serologic surveys in La Guajira yielding attack rates of 13%–93%, an overall laboratory confirmed infection rate of 36%, and an estimated 75,000 human cases and 300 deaths, all occurring within a <4-month interval, underscore the considerable force of epidemic VEE transmission. Reliance on passive reports from hospitals would have led to a considerable underestimate of cases, because native people in the remote rural location of the outbreak frequently avoid established health facilities and privately bury their dead.

Clinical features of cases in the current outbreak were similar to those described previously, with encephalitis occurring mainly in young children and convulsions, the principal neurologic manifestation, developing in 4% of cases overall [14, 15]. Spontaneous abortions and lethal central nervous system malformations in aborted fetuses have been linked circumstantially to VEE infection in previous outbreaks [16, 17]. Our hospital review in Riohacha, which is an underestimate since many women in the area do not seek obstetric care in hospitals, provides further evidence of such an association.

After cases were confirmed in Manaure, the MOH sought to confine the outbreak to La Guajira and to prevent its spread to Magdalena and Cesar States and beyond, where moister environmental conditions could have led to further domestic and potentially international transmission. The rapid institution of active surveillance schemes in all towns in the state provided essential intelligence to guide mosquito control and equine immunization campaigns. The natural corridors formed by the Sierra Nevada de Santa Marta facilitated the restriction of animal movement southward and the creation of an immune barrier through equine immunization. The respective contributions of mosquito control, quarantine, equine immunization, and cessation of rains to the outbreak's subsidence can only be surmised. However, the containment of the outbreak to La Guajira in 1995, in contrast to previous outbreaks, which have spread south to the Magdalena (Tolima State) and Cauca valleys (Valle del Cauca State) and Ecuador, suggests that control measures may have contributed to its cessation [1, 2].

Household surveys and anecdotal reports noted few equine deaths. Donkeys are the principal equine in La Guajira, and few were immunized. Experimental studies have indicated their susceptibility to VEE, although, in the few animals that have been studied, viremias were not consistently of a level infectious to mosquitoes [18]. Several villagers mentioned that goats had died of peste loca. These observations indicate a need for further investigations of vertebrate amplifying hosts in VEE epizootics.

The possibility that humans might act as amplifying hosts has been suggested because VEE viremias are sufficiently high to infect mosquitoes and virus can be isolated from the oropharynx in two-thirds of acutely ill patients, indicating a possibility of direct human-to-human transmission [19]. Although interhuman transmission by *A. aegypti* mosquitoes has been suggested in previous urban VEE outbreaks [20], we found no significant household transmission in the current outbreak. The sine-wave pattern of onset dates is not easily explained but could reflect a synchrony of mosquito feeding behavior. Limiting equine movements has been an important approach in preventing the spread of outbreaks, but our findings do not support a similar need to quarantine people.

The rapidity with which VEE epidemics and epizootics spread precludes effective emergency intervention. The hy-

pothesis that epizootic VEE strains arise by mutation from viruses circulating in sylvatic reservoirs implies the continued periodic emergence of epidemics and epizootics. The institution of systematic equine vaccination, including donkeys, should be resumed to prevent future outbreaks and their considerable morbidity and economic impact.

Acknowledgments

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