NEW LIMITATION CHANGE

TO
Approved for public release, distribution unlimited

FROM
Distribution authorized to U.S. Gov’t. agencies only; Proprietary info.; 23 Nov 1971. Other requests shall be referred to Army Biological Defense Research center, Ft. Detrick, MD 217801.

AUTHORITY

SMUFD, D/A ltr, 18 Feb 1972

THIS PAGE IS UNCLASSIFIED
DISTRIBUTION STATEMENT

Distribution limited to U. S. Government agencies only; proprietary information; statement applied. Other requests for this document must be referred to: Commanding Officer, U. S. Army Biological Defense Research Center, ATTN: Technical Information Division, Fort Detrick, Frederick, Maryland 21701.
I V7

Introduction

Venezuelan encephalitis has appeared in epidemic or endemic forms in the Venezuelan portion of the Guajira, State of Zulia, since autumn of 1930 [3], and has existed in epidemic form for a period not much longer, although there are suspicions that it has been confused with other viral diseases [1]. By 1962 the virus had been isolated from patients in a 1960 epidemic which attacked the Guajira and extended to the eastern end of the country [2, 6]. In October 1968 the region experienced a new outbreak which is analyzed in the present article.

Description of the Epidemic

The affected region. The State of Zulia occupies the northeastern part of Venezuela, between 71 and 73 degrees west longitude and 8.5 to 10 degrees north latitude. The Rez District lies in the northwestern part of the state and borders north and west on the Republic of Colombia, south on the District of the same state, and east on the Gulf of Venezuela. With an area of 3,140 square kilometers, and includes two municipalities: Ciénaga and Puerto Bolivar. In terms of vegetation three zones are distinguished in the region: a forest zone, a pre-desert zone, and a desert zone. The two last zones were the ones most seriously affected by the epidemic; here the temperature is 29 degrees Centigrade in the shade with an annual rainfall less than 500 millimeters (Figure 1). The population estimate for 1968 was 13,130, with an average density of 8 inhabitants per square kilometer. In addition to the populated centers there are numerous widely spaced ranches.

Development of the epidemic. The situation was seen to be abnormal when a significant increase occurred in the number of chicken clucks appearing at the Rural Medical Station in Paraguaná, capital of the municipality of Guajira. An investigation performed around the village uncovered a large number
of diseased horses and a certain number of dead horses. Experience in previous epidemics helped in forming a provisional diagnosis of Venezuelan encephalitis, which was later confirmed by isolation of virus from the blood of several patients.

Isolation and identification of the virus. An attempt was made on serum from the acute phase of febrile patients, on inoculated brains of newborn Swiss white mice and in cultivated cells of Vero strain (ATCC). Fourteen viruses were isolated from 14 inoculated mouse brains. Identification was made in two of the mouse samples, using the following method. Mice were protected. The problem sample was divided in two, one half being mixed parts with serum which was immune to the virus of Venezuelan encephalitis (VEE) (immune horse serum, Lot 1, National Communicable Disease Center, Atlanta, Georgia); the other part was mixed with a phosphate buffer 1/10 of 7.34.

Both mixtures were incubated at 37 degrees C for 1 hour and then inoculated intracerebrally into newborn Swiss white mice. Three mice inoculated with the problem serum which had not been treated with antiserum died 20 hours after inoculation. The mice protected with immune serum were survived for one week and showed no signs of disease whatever.

Serological studies. Twenty pairs of serum, one antiserum convalescent, were studied using Clarke and Casais hemagglutination inhibition test [6] modified by Sever as a microtechnique [7] and employing rabbit serum containing the non-specific inhibitors. In 18 cases there was a clear increase in titer of antibodies to the VEE virus (Table 1).

Criteria for classifying the evidence. Using the criteria employed in 1968 [1], four groups were considered. Group 1 included the cases of patients who showed three or more of the following symptoms: fever, headache, intense headaches, serous-conjunctival congestion, facial paralysis, papilloedema, myalgia, cervical adenopathies, nausea, diarrhea, and vomiting. Group 2 was made up of patients with some of the foregoing symptoms and one or more manifestations such as nystagmus, meningal symptoms, anemia, convulsions, delirium, and delirium. Group 3 consisted of doubtful cases, very mild with indistinguishable from any other febrile condition. These patients were not included in the case studies. Group 4 contained all patients with clearly defined illnesses different from Venezuelan encephalitis.

Distribution throughout time. Figures 2 and 3 show the number of patients consulting the medical stations in Paraguay and the distribution daily beginning on 1 October 1968. A sudden increase can be observed beginning on 27 October and lasting until 1 November. The number of patients at the medical stations began to decline on the day control measures were begun. The epidemic curve for each municipality does not differ from the overall curve for the entire district (Figure 4).

Rate of attack. Table II shows the population of the Pantanal District estimated as of 1 July 1968 and the rate of attack of the illnesses per 1,000 inhabitants. The villages most seriously affected were Marques, La Punta, Los Piludos, Mariches, and El Carite, located in a relatively small area shown

NOT REPRODUCIBLE
in Figure 5. A total of 1,677 symptomatic cases of Venezuelan encephalitis were registered. Of these, 150 showed ulcers in the nervous system. Only two deaths were attributable to the disease in children under one year of age.

Table III shows the distribution of the disease in the age groups by years of age, a fact which can be seen more clearly in Table IV. The mortality rates in population groups above and below 6 years old show that the disease is extremely significant. Among older people the index continues to be progressively smaller. Table V shows the distribution of the disease by sex. In the extreme ages, below one year and above 60, the cases are all male, and the age distribution for females. The other age groups show no significant difference based on sex.

Discussion

The disease has been known in epidemic form in Venezuela since 1936 [4], although Callo and Veglaquez [5] described it in the area in 1930. Encephalitis among humans, however, must have existed in the region since that early, possibly because of confusion with other fevers. According to observations by Avilán [1] the encephalitic epidemics in the region in 1910, 1915, 1916, 1920, 1926-27, 1931, 1939, and possibly late 1940, could have been epidemics of Venezuelan encephalitis. However, in 1950 and 1959, the outbreaks diagnosed as influenza could also have been Venezuelan encephalitis when it is not noted that there were no cases in the area of burro encephalitis [1]. It was not until 1962 that the presence of the Venezuelan encephalitis virus was confirmed in patients during an epidemic which occurred in the region [6].

The fact that the mortality rate in children under 6 years of age indicates that the virus has not been present in the population since the epidemic of 1962. This agrees with reported observations (to be published) on the absence of antibodies against Venezuelan encephalitis among children under 5 years of age in the Guairía in 1971. Furthermore, the history of the disease in the area, it can be concluded that there is a cyclic activity and that there are no cases of the disease in the years between epidemics.

Some authors [3, 4] have reported that the apparent passive disappearance of a certain type of antibodies in individuals who have suffered Venezuelan encephalitis. But the epidemiological evidence shows that this apparent loss not modify the acquired resistance of the population. It is observed that mortality rates are progressively lower over higher ages, and this, in a population uniformly exposed to the causative agent, is a demonstration of immunity. Furthermore, one can observe resistance diminution in children under one year old, which can be explained in terms of transmitted maternal antibodies. It can be concluded from the foregoing that the disease confers long-lasting immunity.

In addition to the 1,677 cases examined clinically, there were around 500 consulting patients with febrile conditions which were not diagnosed as Venezuelan encephalitis because they did not meet the established criteria but

NOT REPRODUCIBLE
who probably had very benign cases of the disease. According to Ryder (in
publication) it is also probable that similar subclinical infections caused by
this virus, since high titres of antiviral antibodies were found in
zones where no epidemics of Venezuelan encephalitis were described, such as
the region to the south of Lake Maracaibo. Some cases of the disease
must have been much greater than the actually recorded.

The serious neurological cases, however, constituted a low per cent of the total of pa-
tients, a high percentage in contrast to the epidemics in which the level
was calculated at 6%. If we include those cases only of consulting pa-
tients placed above in group 3, we arrive at a value of 1% of neurological
cases, a number which is in any case higher than that for children. The number of
deaths attributable to the disease was 0.1%, of the deaths much lower than the
figure for the previous epidemic [3].

No logical explanation was found for the marked difference for females
among children less than one year old and among those over 40. It should
be noted that the difference was observed only in males.

Summary

An epidemic of Venezuelan encephalitis, which occurred in October 1968
in the District of Fene, State of Zulian, was described here. A total of
1,077 cases of the disease were registered, including evident attack
on the nervous system. Two deaths were attributed to the encephalitis,
both in children less than one year old. There was a large number of cases
among children less than 6 years old; this was the region of the last encephali-
is epidemic in the region, which points to a high reactivity of the virus.
It was concluded that the virus is inactive in known epidemic periods. The
immunity conferred by the virus is apparent in these periods, as indicated
by the small number of older patients and in children less than one year old,
the latter protected by transmitted material immunity.


NOT REPRODUCIBLE
FIGURE CAPTIONS

Figure 1. Map of the District of Rix, showing settlement affected by the outbreak.

Figure 2. Number of consultants at the Tumaco Station of Paramusipoa beginning on 1 October 1968. The first wave of the outbreak on 27 October is visible.

Figure 3. Number of consultants at the Tumaco Station of Sina during the same period. Although there is a rise in the number of febrile cases, the number of convulsive cases is much lower. (Febrile: --, neurological --, total: --)

Figure 4. Epidemic curve for the two municipalities. The epidemic affected primarily the municipality of Octubre. The Municipality of Sina participated in the curve. (Paramusipoa --, Sina --, Octubre --)

Figure 5. Map of the District, showing the severely affected region. The region in black registered approximately 1,077 cases. The villages in the gray region reported between 200 and 500 cases. The rest of the 1,077 cases were found in the checked region.

Spanish Words Used in Figures

<table>
<thead>
<tr>
<th>Spanish Word</th>
<th>English Meaning</th>
</tr>
</thead>
<tbody>
<tr>
<td>total</td>
<td>total</td>
</tr>
<tr>
<td>febril</td>
<td>febrile</td>
</tr>
<tr>
<td>neurologicos</td>
<td>neurological</td>
</tr>
<tr>
<td>consultantes</td>
<td>consultants</td>
</tr>
<tr>
<td>Octubre</td>
<td>October</td>
</tr>
<tr>
<td>Noviembre</td>
<td>November</td>
</tr>
<tr>
<td>Casos</td>
<td>cases</td>
</tr>
<tr>
<td>Tipos I y III</td>
<td>Types I and III</td>
</tr>
</tbody>
</table>
### TABLA I

**Títulos de anticuerpos inhibidores de la hemaglutinación contra el virus EEV en 20 pacientes.**

<table>
<thead>
<tr>
<th>NOMBRE</th>
<th>EDAD</th>
<th>SUERO AGUDO</th>
<th>SUERO LÓVENALECIENTE</th>
</tr>
</thead>
<tbody>
<tr>
<td>L.G.A.</td>
<td>10</td>
<td>&lt;10</td>
<td>&gt;1200</td>
</tr>
<tr>
<td>N.M.</td>
<td>50</td>
<td>&lt;10</td>
<td>160</td>
</tr>
<tr>
<td>N.O.</td>
<td>14</td>
<td>&lt;10</td>
<td>160</td>
</tr>
<tr>
<td>E.D.</td>
<td>30</td>
<td>&lt;10</td>
<td>160</td>
</tr>
<tr>
<td>E.G.</td>
<td>35</td>
<td>&lt;10</td>
<td>160</td>
</tr>
<tr>
<td>A.A.</td>
<td>26</td>
<td>&lt;10</td>
<td>&lt;10</td>
</tr>
<tr>
<td>A.V.</td>
<td>25</td>
<td>&lt;10</td>
<td>160</td>
</tr>
<tr>
<td>P.P.</td>
<td>10</td>
<td>&lt;10</td>
<td>160</td>
</tr>
<tr>
<td>V.M.</td>
<td>5</td>
<td>&lt;10</td>
<td>160</td>
</tr>
<tr>
<td>A.I.</td>
<td>24</td>
<td>&lt;10</td>
<td>160</td>
</tr>
<tr>
<td>N.G.</td>
<td>17</td>
<td>&lt;10</td>
<td>160</td>
</tr>
<tr>
<td>M.G.</td>
<td>29</td>
<td>&lt;10</td>
<td>&gt;1200</td>
</tr>
<tr>
<td>I.G.</td>
<td>11</td>
<td>&lt;10</td>
<td>320</td>
</tr>
<tr>
<td>I.G.</td>
<td>10</td>
<td>&lt;10</td>
<td>320</td>
</tr>
<tr>
<td>F.F.</td>
<td>20</td>
<td>&lt;10</td>
<td>&gt;1200</td>
</tr>
<tr>
<td>J.G.</td>
<td>25</td>
<td>&lt;10</td>
<td>320</td>
</tr>
<tr>
<td>C.C.</td>
<td>13</td>
<td>&lt;10</td>
<td>320</td>
</tr>
<tr>
<td>M.M.</td>
<td>30</td>
<td>&lt;10</td>
<td>&lt;10</td>
</tr>
<tr>
<td>V.G.</td>
<td>5</td>
<td>&lt;10</td>
<td>320</td>
</tr>
<tr>
<td>R.A.</td>
<td>-</td>
<td>&lt;10</td>
<td>320</td>
</tr>
</tbody>
</table>

### TABLA II

**Encefalitis equina venezolana. Distrito Páez, Estado Zulia. 1966. Relación de casos por municipios. Tasas de ataque por 1,000 habitantes.**

<table>
<thead>
<tr>
<th>MUNICIPIO</th>
<th>POBLACION</th>
<th>NUMERO DE CASOS</th>
<th>CASOS POR 1,000</th>
</tr>
</thead>
<tbody>
<tr>
<td>Guajira</td>
<td>13,937</td>
<td>957</td>
<td>68,7</td>
</tr>
<tr>
<td>Sinamaca</td>
<td>4,459</td>
<td>120</td>
<td>26,9</td>
</tr>
<tr>
<td>Distrito Páez</td>
<td>18,394</td>
<td>1,077</td>
<td>58,4</td>
</tr>
</tbody>
</table>

Para el 1º de julio de 1966.
### Table I

1. **Titres of antibodies inhibiting hemagglutination against the VEE virus in 20 patients**
2. Name
3. Age
4. Acute serum
5. Convalescent serum

### Table II

1. **Venezuelan equine encephalitis, Paez District, State of Zulia, 1968. Numbers of cases by municipalities and rates of attack per 1,000 inhabitants**
2. Municipality
3. Estimated population
4. Number of cases
5. Cases per 1,000 inhabitants
6. As of 1 July 1968

### Table III

1. **Distribution of cases by age groups. Rates of attack per 1,000 inhabitants**
2. Age groups
3. Guajira Municipality
4. Sinamaica Municipality
5. Paez District
6. Cases
7. Estimated population
8. Rate
9. Up to one year old
10. One to 6 years old
11. Forty and older
12. Age unknown
13. Total

### Table IV

1. **Differences in mortality rates between those above and below 6 years of age**
2. Age groups
3. Guajira Municipality
4. Sinamaica Municipality
5. Paez District
6. Cases
7. Estimated population
8. Rate
9. Less than 6 years old
10. Over 6 years old
Table V

1. Distribution of cases by age groups and estimated incidence of attack per 1,000 inhabitants
2. Age groups
3. Guajira Municipality
4. Sinu Municipality
5. Tocaz District
6. Cases
7. Estimated population
8. Rate
9. Up to one year old
10. One to 6 years old
11. Forty and older
12. Age unknown
13. Total
V Male
M Female

2641
CSO: T-798-W