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SITUATION OF EQUINE ENCEPHALITIDES IN THE AMERICAS 1989-1994

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PAN AMERICAN HEALTH ORGANIZATION
Pan American Sanitary Bureau, Regional Office of the
WORLD HEALTH ORGANIZATION

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Division of Disease Prevention and Control
VETERINARY PUBLIC HEALTH PROGRAM

EQUINE ENCEPHALITIDES SITUATION IN THE AMERICAS 1989-1994

INTRODUCTION

Equine encephalitides are viral zoonoses transmitted by mosquitoes that occur seasonally, causing outbreaks in equines and, less commonly, illness in humans.

The causative agent belongs to the *Alphavirus* genus of the Togaviridae family. Three viruses of this genus are important because they cause disease in both solidungulates and in humans: eastern equine encephalitis (EEE); western equine encephalitis (WEE); and Venezuelan equine encephalitis (VEE). A fourth member of this genus, the Highlands J. virus, has been reported only in the eastern portion of the United States, especially in Florida, and is associated with cases of equine encephalomyelitis (2).

Each of these viruses has a wild cycle that includes certain vertebrates and various vectors, particularly mosquitoes.

The clinical signs and histopathological changes observed in equine encephalitides in both humans and animals are similar; this is not the case, however, with regard to morbidity and mortality, which vary in accordance with the type of infection.

Eastern Equine Encephalitis (EEE)

The EEE virus occurs in North, Central, and South America, with antigenic variations in the different regions and transmission by different vectors.

In the eastern part of the United States, the virus is transmitted by the *Culiseta melanuria* mosquito and circulates permanently in birds, especially in swampy areas. In other areas, it has been found in the *Aedes sollicitans,* a mosquito that abounds in marshy regions with brackish water and that transmits the virus to birds, equines, and humans. In tropical countries in the Americas, the principal vectors are *Aedes taeniorhynchus, Culex nigripalpus, Culex taeniopus, Culex panacossa* and *Culex dunni* (1)

Humans and equines are accidental hosts and terminal points in the chain of transmission.

This form of encephalitis is not frequent in humans but has a high case-fatality rate of nearly 50% and may leave permanent sequelae of varying severity in children under 5.

The case-fatality rate in horses with signs of encephalitis is on the order of 75-90%. The EEE virus also causes high mortality in pheasants. An association has been confirmed between the occurrence of human and equine cases of EEE and excess rainfall.

Western Equine Encephalitis (WEE)

The WEE virus is found in the United States, Canada, Mexico, and some South American countries. In the United States the Central Valley of California is recognized as an endemic area where sporadic outbreaks occur, but the disease also exists in other parts of the country.

Cases in equines tend to occur sporadically at the beginning, subsequently acquiring epizootic characteristics.

The principal vector in the United States is *Culex tarsalis* and possibly *Aedes dorsalis* (8). In the eastern part of the country, the vector is *Culiseta melanuria*, an essentially ornithophilic mosquito, which would explain the absence of human cases and the low frequency in equines.

The natural reservoirs of the WEE virus are birds, especially passeriformes, which develop a brief viremia of 2-5 days, during which time the mosquitoes are infected by feeding on them (2). The birds maintain the virus in nature up to 10 months after infection. The hosts who develop disease are humans and horses. The mortality rate in humans ranges from 5% to 10% and from 10% to 50% in solidungulates.

Venezuelan Equine Encephalitis (VEE)

The VEE virus has been verified only in the Americas and has been recognized as a causative agent of equine encephalitis since 1938.

Large-scale epizootics of the virus occurred in Colombia, Venezuela, Trinidad, and Peru between 1955 and 1959. In 1967, there was an outbreak in various regions of Colombia extending to Peru, Ecuador and, in 1969, to the Central American Isthmus, where it affected all the countries except Panama, finally reaching Mexico and Texas in the United States in 1971.

The VEE virus has six subtypes, I to VI, as indicated in Table 1. It was formerly believed that the enzootic subtypes and variants are not pathogens for solidungulates, immunizing them against epizootic variants. However, this hypothesis is about to be revised, given the variability and mutagenicity of the viruses, which can give rise to new epizootic variants. In 1993, an epizootic occurred in Mexico; the virus was isolated and characterized as 1E, known to be enzootic.

The wild cycle is observed in the humid rain forests of the tropical regions of the Americas and in swampy areas where viral transmission is enzootic and develops among rodents and several species of mosquitoes of the genus *Culex*. Humans may be infected when they enter an enzootic ecosystem. The epizootic cycle is maintained between equines and several equinophilic mosquitoes. In humans, infection with enzootic strains can produce disease and even death, when there is exposure to mosquito vectors in the natural environment (1).

Epizootics are produced by viruses of variants A, B, and C, subtype I. They tend to be explosive and dramatic. The infection in solidungulates can reach extreme proportions approaching 100%, and mortality can occur in from 20% to 40% of the total population, with a case-fatality rate of from 38% to 83%. (9)

Table 1

CLASSIFICATION THE VIRAL COMPLEX OF VENEZUELAN EQUINE ENCEPHALITIS (VEE)

SUBTYPE	VARIANT	REPRESENTATIVE STRAIN	ACTIVITY	ORIGIN
I VEE	A	TC 83	Vaccine	Derived from burro, Trinidad
	A	Burro Trinidad	Epizootic	Burro, Trinidad
	B	MF-8	Epizootic	Human, Honduras
	C	P-676	Epizootic	Horse, Venezuela
	D	3380	Enzootic	Human, Panama
	E	Mena II	Enzootic	Human, Panama
	F	78V-3531	Enzootic	Mosquito, Brazil
II Everglades		Pe-3-7c	Enzootic	Mosquito, Florida
III Mucambo	A	Mucambo	Enzootic	Monkey, Brazil
	B	Tonate	Enzootic	Bird, French Guiana
	C	71D-1252	Enzootic	Mosquito, Peru
IV Pixuna		Pixuna	Enzootic	Mosquito, Brazil
V Cabassou		Cabassou	Enzootic	Mosquito, French Guiana
VI		AG-80-663	Enzootic	Mosquito, Argentina

* Taken from C. San Martín. Encefalitis equina ocasionada por virus transmitidos por artrópodos. ICA informational material, Colombia

Venezuelan equine encephalitis in humans is commonly manifested in undifferentiated febrile and benign disease accompanied by headache, myalgia, pharyngitis, and leukopenia with lymphopenia. Clinical cases usually occur in 11% to 20% of the general population but may reach much higher figures. Mortality is low and has been estimated at between 0.2% and 1.0% of clinical cases. An 4% incidence of encephalitis has been observed in children and 0.4% in infected adults. In an epidemic in the Guajira region of Venezuela, birth defects, including anencephalia, were observed in the fetuses of mothers who had contracted the

disease during pregnancy.

Various vectors are involved in the epizootics: *Psorophora confinnis, Psorophora discolor, Mansonia titillans, Mansonia indubitans, Aedes taeniorhynchus, Aedes sollicitans, Aedes scapularis, Aedes theleter, Deinocerites pseudes*. The isolates of the virus obtained from *Aedes aegypti* suggest that it may be a vector in person-to-person transmission (1).

Other animals may be infected during epizootics, such as cattle, pigs, and dogs can be infected but the disease has been confirmed only in dogs.

Equine cases usually precede human cases, and they decline and cease when the population of susceptible solidungulates that maintains the vector infection is exhausted.

SITUATION OF EQUINE ENCEPHALITIDES IN LATIN AMERICA AND THE CARIBBEAN

General Considerations

In the past 15 years, surveillance of equine encephalitides has declined in most of the countries of Latin America and the Caribbean, so much so that the situation of these diseases is unknown at the present time. The few countries that report clinical cases consistent with equine encephalitides obtain no laboratory confirmation. In Latin America and the Caribbean, laboratory diagnosis of equine encephalitides has practically ceased. There are only six countries in the Americas with the facilities to perform laboratory diagnosis of equine encephalitides; however, the laboratories located in Latin American countries have technical limitations with respect to isolating and typing the virus (see Table 2). The Centers for Disease Control and Prevention (CDC) at Fort Collins is subject to restrictions on receiving samples of infectious material from other countries and consequently is unable to provide international reference services.

Table 2

LABORATORIES IN THE AMERICAS THAT DIAGNOSE EQUINE ENCEPHALITIDES, 1994

COUNTRY	LABORATORY	TECHNIQUE UTILIZED
Argentina	. Instituto de Virología,Córdoba Province	. Isolation . Serology
Brazil	. Instituto Adolfo Lutz, Sao Paulo	. Isolation . Serology
Colombia	. Instituto Colombiano Agropecuario, Bogotá	. Serology
Mexico	. Instituto de Investigaciones Pecuarias (INIP), Palo Alto	. Serology . Isolation
Venezuela	. Instituto de Investigaciones Veterinarias, Maracay . Instituto Nacional de Higiene, Caracas	. Isolation . Serology . Isolation . Typing . Serology
United States	. Centers for Disease Control and Prevention (CDC) Reference Laboratory for Arboviral Disease, Fort Collins	. Isolation . Typing . Serology . Viral characterization

Some countries have continued to utilize the weekly information system of the Pan American Foot-and-Mouth Disease Center (PANAFTOSA), which reports by quadrants the occurrence of syndromes consistent with equine encephalomyelitis of viral origin, locating the site of occurrence in the coordinates of every country.

Table 3 presents a summary of the information received from the countries during the period 1989-1994. The limited participation of the countries is evident, since only Argentina, Bolivia, Brazil, Colombia, Ecuador, El Salvador, Guatemala, Paraguay, and Venezuela reported. In 1994, Panama and Peru started reporting. (7), (8).

Of the countries listed, only Colombia has sent all its weekly reports since 1989.

Table 3

OCCURRENCE OF REPORTED FOCI OF SYNDROMES CONSISTENT WITH EQUINE ENCEPHALITIDES AND NUMBER OF WEEKS REPORTED, 1989-1994

COUNTRY	YEARS					
	1989	1990	1991	1992	1993	1994
Argentina	0/10 (1)	2/52	3/52	N/I (2)	N/I	N/I
Bolivia	N/I	6/31	0/49	0/52	0/52	0/46
Brazil	0/2	8/41	3/41	4/52	3/49	2/52
Colombia	2/13	11/52	8/53	28/53	7/52	19/52
Ecuador	N/I	N/I	0/20	0/52	1/52	0/52
El Salvador	N/I	10/9	11/19	23/24	7/27	N/I
Guatemala	0/1	1/36	8/53	3/46	2/52	0/51
Panama	N/I	N/I	N/I	N/I	N/I	0/11
Paraguay	0/9	0/21	0/52	0/50	0/52	0/52
Peru	N/I	N/I	N/I	N/I	N/I	1/15
Venezuela	0/5	2/49	0/46	4/52	7/52	0/52

(1) Number of occurrences of foci/number of weeks reported

(2) Did not report (NI)

Source: Pan American Foot-and-Mouth Disease Center (PANAFTOSA)

With the limited information furnished during the period October 1989-December 1994, it has been possible to confirm the existence of enzootic areas in various countries where clinical episodes of equine encephalitides were frequently reported. As an example, Table 4 and Figures 1, 2, and 3 show the location of these areas in some countries. The distribution and size of these areas is only an approximation, since more complete information is not available.

During the period 1993-1994, some changes in the epidemiological situation of some of the countries were observed, while, other countries, such as Brazil, El

Salvador, and Venezuela continued to present foci in the same enzootic areas. In Colombia, foci of encephalitic disease occurred in equines in two localities not reported previously. One of the new enzootic regions is the junction of the Meta, Ariporo, and Cravo Norte rivers, where foci were reported in week 23 of 1993. The other new region is located in Tumaco, Department of Nariño. In this same country, greater activity was noted during 1994, particularly during the months of August and November.

Guatemala continued to report foci in the enzootic area of Mita and Lake Guija, but foci were also reported in Petén and on the northwestern bank of the Motagua River on the Honduran border.

As in previous years, the reports of foci of equine encephalitis syndrome do not specify the number of affected or dead animals nor the type of virus involved.

Table 4

ENZOOTIC LOCATION OF CLINICAL SYNDROMES CONSISTENT WITH EQUINE ENCEPHALITIDES REPORTED IN FIVE COUNTRIES 1989-1994

COUNTRY	AREA NO.	QUADRANTS INVOLVED	LOCATION
Brazil	1	2966-2967-2968-3064-3067	Near Urquirim Dam, Sao Paulo State
	2	3168-3169-3170	Municipios of Jacupiranga, El Dorado, and Cananeia, Sao Paulo State
	3	1373-1374-1474	Municipio of Floriano, Piaui State
	4	1077-1178	Municipios of Fortaleza, Cascabel, and Pacajus, Ceará State
Colombia	1	1039-1139-0939	Urabá and Río Atrato region, Departments of Antioquía and Chocó.
	2	0840-0841-0741	Cienaga de Oro, Lorica, Montería, Coveñas and Tolú region, Departments of Córdova and Sucre
	3	0742-0641	Magangué, El Banco, and Calamar, Department of Bolivar
	4	1443-1444-1343	Magdalena Medio, La Dorada, Honda, Pto. Salgar, and Ginadot, Departments of Caldas, Cundinamarca, and Tolima
	5	1249	El Sarare region, Arauca
El Salvador	1	0522-0523-0423-0720	San Cristóbal region, Border with Guatemala, Department of Santa Ana.
	2	0325-0326	Metapán, Department of Santa Ana.
	3	0529-0530-0430	Dulce Nombre de María region, Department of Chalatenango.
	4	0831-0832-0833-0834-0732-0734	Department of Cabañas.
Guatemala	1	2643	Region from Mita to Lake Guija, Border with El Salvador.
	2	2346*	Border with Ahuachapán, El Salvador.
Venezuela	1	E06-E07-F06	Eastern shore of Lake Maracaibo, Trujillo State, Zulia State.
	2	E04-E05	Mara and Paez districts, Zulia State
	3	D07	La Carora and San Francisco, Lara State

PROPOSAL FOR REACTIVATION OF REGIONAL EPIDEMIOLOGICAL SURVEILLANCE OF EQUINE ENCEPHALITIDES

The reactivation of epidemiological surveillance requires a joint coordinated effort by the health and agricultural sectors of the countries with the active participation of the owners of equine livestock and the international technical cooperation agencies. The system should coordinate the various activities aimed at timely collection and analysis of data on the behavior of the disease and the factors that determine its prevalence, ensuring that the information is available. The lack of laboratory confirmation of the diagnosis makes this a priority consideration in reactivating epidemiological surveillance of equine encephalitides.

1. Strengthening of laboratory diagnosis

1.1 All the countries that have reported cases or outbreaks of equine encephalitides in the past, particularly VEE, should develop diagnostic laboratories, including facilities for viral isolation and serology. Among such countries are Brazil, Colombia, Venezuela, Ecuador, El Salvador, Guatemala, Honduras, Mexico, Nicaragua, Peru, and Costa Rica.

1.2 Countries bordering those containing endemic areas should have serological techniques available for the diagnosis of the three equine encephalitides: VEE, EEE and WEE. The countries in question are Argentina, Uruguay, Bolivia, Paraguay, Panama, Guyana, Suriname, and Dominican Republic.

1.3 Four reference laboratories will be set up with the capability of performing viral isolation and viral typing. The host country should be flexible in permitting the entry of samples of biological material for making reference diagnoses. These laboratories, moreover, should produce and distribute reference materials (antigens, sera) to the laboratories of other countries and should also provide facilities to train personnel through course offerings or in-service training.

The reference laboratories should organize and maintain a collection of strains from the isolates made within the country and in other countries of the Region for which it has provided diagnostic services. This will points to the need to develop monoclonal antibody and genetic sequencing techniques for viral characterization.

It is proposed that these laboratories be located and provide the aforementioned services as follows:

.	Brazil	Support for countries of the Southern Cone
.	Colombia	Support for countries of the Andean Area and Panama
.	Mexico	Support for countries of Central America
.	Venezuela	Support for countries of the Caribbean

2. Epidemiological Surveillance

Epidemiological surveillance activities are aimed at early detection of encephalitis viral activity in order to predict and prevent epizootics and human cases.

The most common sign of the imminence of an outbreak of equine encephalitis is the appearance of clinical cases in the solidungulates and, in the case of VEE, an increase in febrile diseases in humans. The possibility of epizootics depends on the epidemiological characteristics of each of the encephalitides and of the proportion of the equine population that is immune to the particular virus.

Some elements are considered fundamental for implementing the epidemiological surveillance system for equine encephalitides.

2.1 Epidemiological Characterization

Venezuelan equine encephalitis (VEE) is the disease that causes the greatest concern, in view of its high morbidity and case-fatality in

solidungulates and its importance as a pathogen for humans. The potential for epizootics of this encephalitis and its prevention through equine vaccination suggests the need for defining the populations at risk. It is to be expected that the regions where epizootic activity has occurred will again be the scene of new outbreaks when time has replaced the immune survivors of the equine population with susceptible animals. Experience shows that maps such as those based on the Holdrige system make it possible to identify the regions where epizootic outbreaks are likely to occur and likewise, those that will remain unaffected.(8) (12)

It will be necessary in these areas to determine the human and equine populations at risk and to identify the possible vectors of the virus.

Complementary serological studies can define the proportion of susceptible horses in an area and serve as the basis for planning vaccination campaigns. (10)

2.2 Reporting and Investigation of Cases and Outbreaks

The surveillance system will become operational when the level of awareness is raised in the public and private veterinary services and the population at large of the importance of reporting any case or outbreak of equine disease with encephalitic symptoms. Achieving this requires the development of a broad training program in the veterinary services in epidemiology and the clinical manifestations of equine encephalitides and in the collection and transmission of samples to the laboratories. It will also be necessary to undertake community-directed educational programs.

It is important to determine and differentiate normal or endemic disease situations from epizootics requiring an epidemiological alert, and for this purpose veterinarians in a given area should familiarize themselves with epidemiological research methodology and the evaluation of disease frequencies. Research should provide information on the boundaries of the epizootic ecosystem and will serve as a guideline for the implementation of control measures (10), (12).

2.3 The Information System

Equine encephalitides are reportable diseases, and the countries should therefore have a system for the systematic collection of data and the consolidation, evaluation, and timely distribution of the information, especially to the decision-making levels and other levels that require such information in order to take action.

The weekly information furnished by the quadrant system is useful and should continue, but foci should be monitored in order to provide useful additional information on the evolution of the disease and permit the timely forecasting of epizootics.

The system should establish adequate flows of information that will make it possible to register reports of suspected cases of disease and death from encephalitis in horses, mules, and donkeys, in addition to establishing the channels for performing laboratory tests that will confirm the presence of the disease.

A data bank should be maintained with information by departments or states, on properties, concentrations of livestock and vaccination coverage (race-tracks, clubs, cavalry posts) populations by species, age categories, types of animal production, trade and livestock fairs, production laboratories and vaccine dispensaries, as well as registries of personnel and their degree of training. Based on regional information, it will be necessary to maintain maps of the properties affected according to the type of diagnosis (clinical, pathological, serological, virological) and the flow of animals according to destination (farm, market, fair, slaughterhouse) (11).

Finally, matters relating to information and surveillance of encephalitides should be coordinated with local and national entities in the health sector.

2.4 Sentinel Animals

The use of sentinel animals can provide information on the transmission activity of the Venezuelan equine encephalitis virus.

The selection of areas will be made by taking into account retrospective studies containing information on previous outbreaks of VEE in localities that at the present time show no viral activity, high levels of antibodies in the equine population, the presence of IgM antibodies against VEE, or localities that have recently reported cases of equine disease. The cooperation of the owners of solidungulates is essential. Hamsters have demonstrated their suitability for detecting viral activity. Unvaccinated solidungulates free of antibodies and coming from areas with no history of encephalitis may also be used (9) (12).

The use of sentinel animals may be combined with the detection and isolation of the virus in vector species of the area, once viral activity has been found in the sentinel animals.

2.5 Research

Research is a useful for gaining knowledge about any epidemiological process, especially the multiple interactions of an agent with its hosts and the environment that surrounds it.

In equine encephalitides, studies should be made of the virus itself, its variants, and its relation to epizootic and enzootic manifestations. There is a need to determine the variants of the VEE virus in the different ecosystems and their potential virulence for causing epizootics. Knowledge about the stability of the TC-83 vaccinal virus and the homogeneity of the strains used in the vaccine-producing laboratories will also be necessary. Finally, the effectiveness of the TC-83 vaccine strain isolated in 1943 in combatting the variants of the VEE virus currently active in the field, as well as the length of the immunity that this vaccine confers in vaccinated horses must be ascertained (8).

2.5.1 Viral Characterization

Viral isolation is necessary for comparing the characteristics of the viruses associated with endemic and epidemic transmission and with the clinical disease in humans and solidungulates.

For the purposes of isolation, blood and tissue samples from infected equines and members of their herd that are in febrile state can be utilized, as well as blood or tissue from sentinel animals and vector mosquitoes.

Viral characterization molecular biotechnology techniques that can be carried out only in a specialized laboratory such as the WHO Reference Center for arboviruses of the CDC at Fort Collins or the U.S. Army Medical Research Institute for Infectious Diseases (USAMRIID), in Fort Detrick.

2.5.2 Antigenic Characterization of the Vaccine Strain

A vaccine from attenuated live virus (TC-83) is available at the present time that has yielded satisfactory results in immunizing equines. The viral strain was isolated from a burro in Trinidad in 1943 and attenuated by passages in the fetal heart cells of guinea pigs until passage 83, which is used for the production of the vaccine. To date, no information is available on the possible reversion of the vaccine virus, but the possibility has still not been ruled out. The availability of techniques for the genomic characterization of the viruses will make it possible to compare the TC-83 strain isolated in 1943 with the strain utilized today in the vaccine-producing laboratories and with the enzootic and epizootic strains of VEE.

"Fingerprinting" of oligonucleotides has shown a relationship between some isolates in certain geographical areas (11). However, these studies have technical limitations, since they do not permit a thorough characterization of the viral genome.

In addition, it is suggested that the changes in the adaptability of epizootic and enzootic viruses may produced, through mutation, new subtypes of the Venezuelan equine encephalitis virus, a conjecture that merits research into the protective effects of TC-83 against these mutants.

2.5.3 Post-vaccinal Immunity of Equines to VEE

Since the TC-83 vaccine is an attenuated live strain, the assumption is that it can confer lifelong immunity. At the present time, the length of immunity produced in a vaccinated animal is unknown.

Studies at the Instituto Colombiano Agropecuario in 1971 revealed that horses maintained antibodies and resisted the assaults of epizootic viruses for as long as 30 months after vaccination with the TC-83 strain. (3)

3. Intersectoral Collaboration

The economic implications of equine encephalitides for equines, as well as the public health risks, demonstrate the need for joint work between the agricultural and health sectors to develop epidemiological surveillance of this complex of diseases.

The formation of national and local zoonosis committees has been of value in some countries in defining the responsibilities of each sector and pooling human and financial resources for the implementation of encephalitides surveillance and prevention programs.

4. Community Participation

The importance has already been mentioned of the role that livestock producers and farmers should play in the timely reporting of cases or outbreaks of encephalitic disease in equines as a means of promoting the effectiveness of the information and epidemiological surveillance systems.

The community should be properly motivated to collaborate in national programs for the surveillance, prevention, and control of diseases, which suggests the need to develop extensive and comprehensive programs for education and information dissemination.

The educational components should include not only elements related to equine encephalitides and epidemiological surveillance but components that motivate the community to participate in prevention and control activities such as vaccination campaigns.

Simultaneous development of all the elements referred to above for the reactivation of epidemiological surveillance of equine encephalitides will not be possible in all the countries, and therefore, priorities must be set.

In the meantime, it is recommended that all the countries in the Americas participate in the weekly information system on clinical syndromes consistent with equine encephalitides. Countries with endemic areas should make an effort to develop laboratory diagnosis capabilities and carry out studies aimed at epidemiological characterization of equine encephalitides that will facilitate the adoption of effective prevention and control measures.

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Figure 1

BRAZIL

Occurrence of Foci of Syndromes Consistent with Equine Encephalitides. 1989-1994

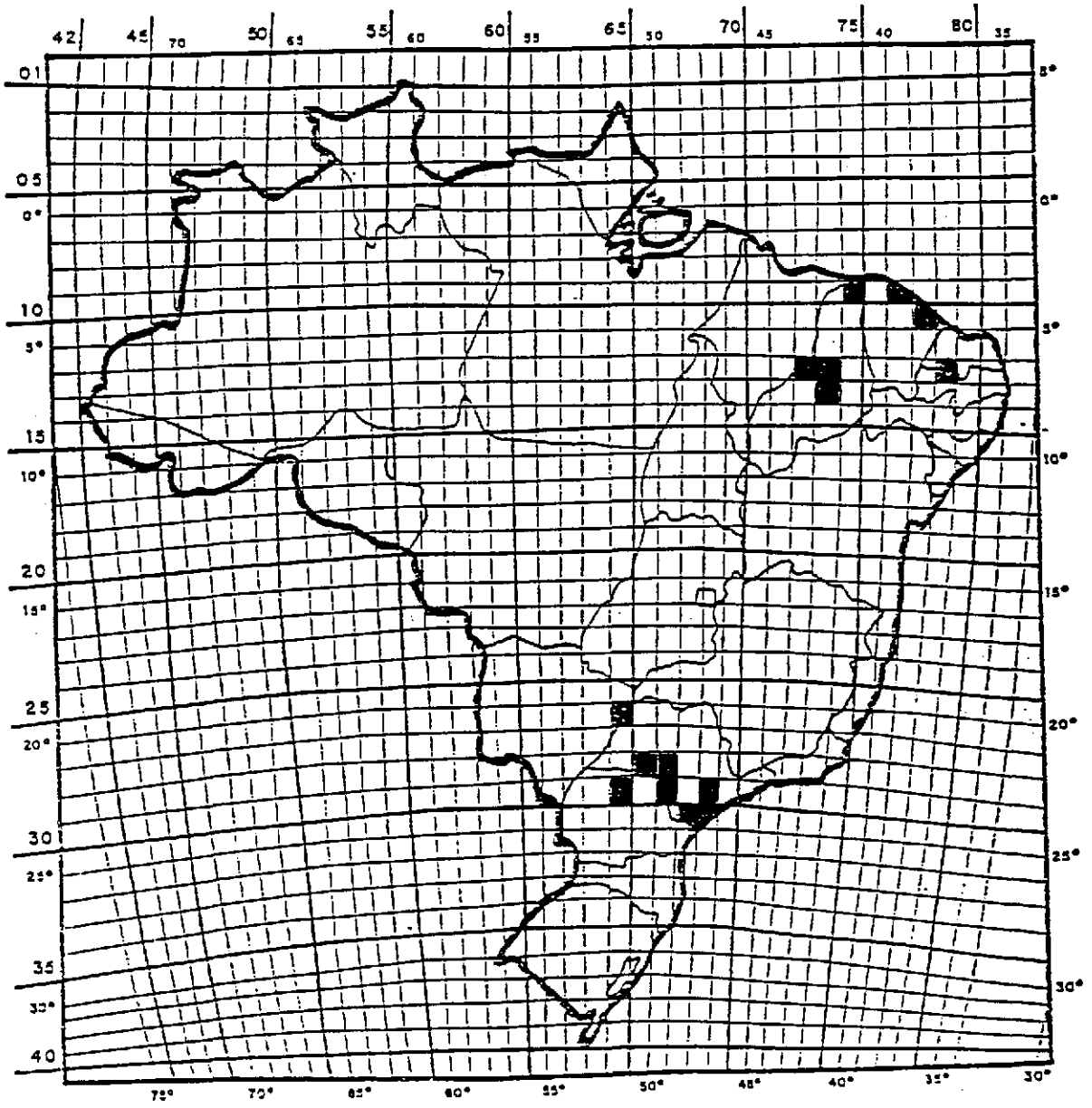
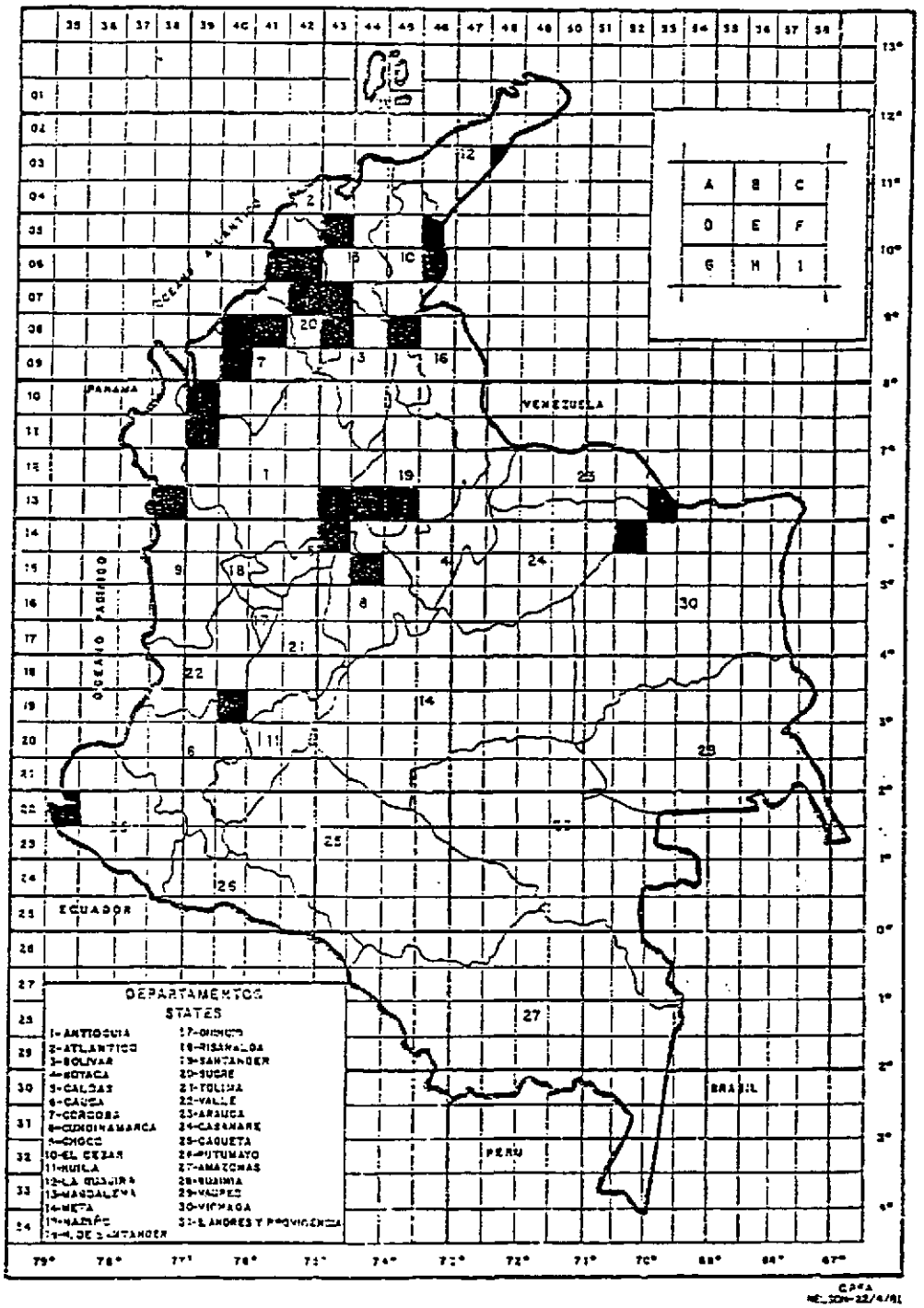


Figure 2

COLOMBIA

Occurrence of Foci of Syndromes Consistent with Equine Encephalitides. 1989-1994

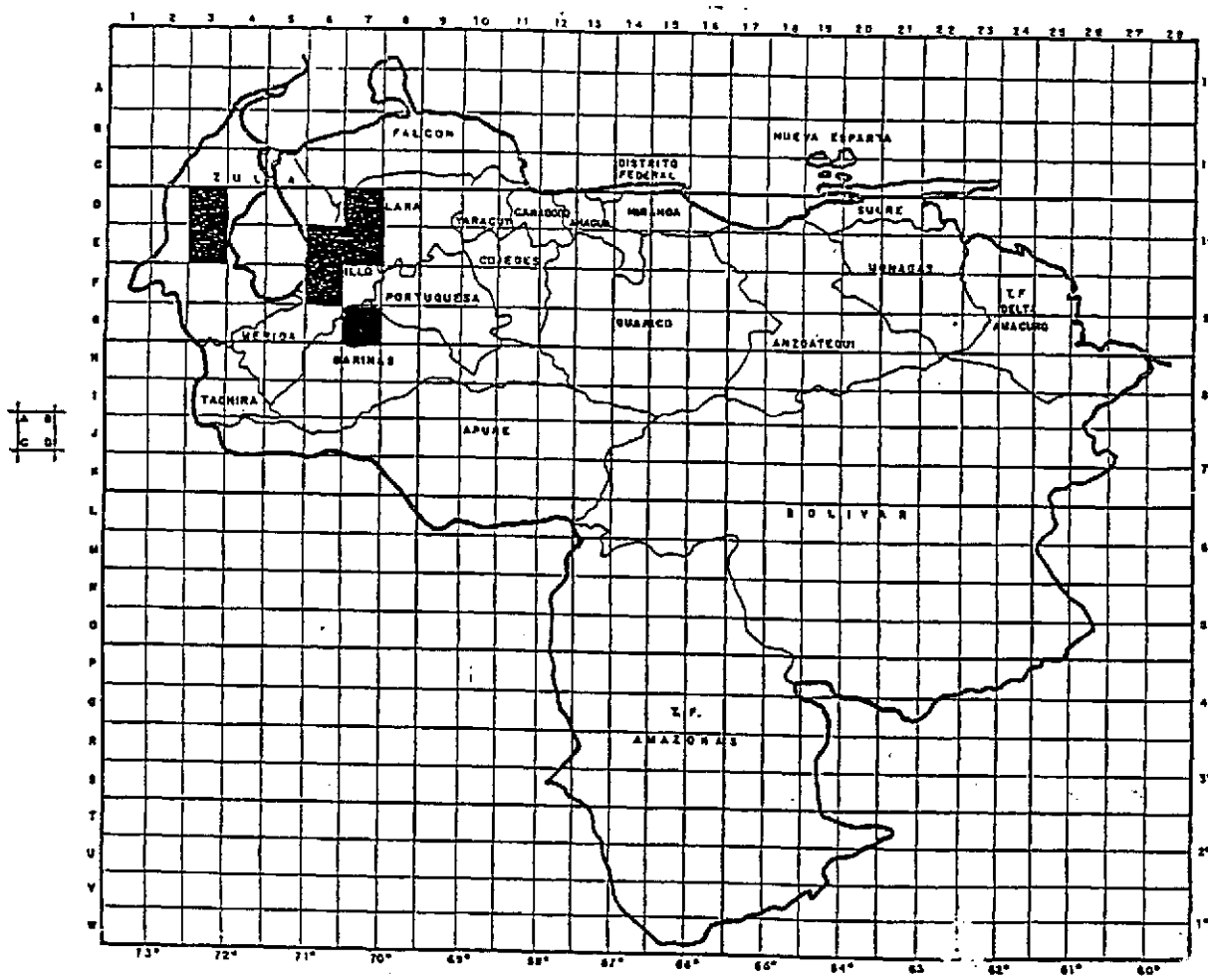


1 VEE confirmed by laboratory

Figure 3

VENEZUELA

Occurrence of Foci of Syndromes Compatible with Equine Encephalitides, 1989-1994



1 VEE confirmed by laboratory