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CONTROL AND ERADICATION OF AEDES AEGYPTI

The 95th Meeting of the Executive Committee of the Pan American Health Organization held at the Headquarters of the Organization in Washington D.C., from 24 to 28 June 1985, approved the inclusion in the Provisional Agenda of the XXXI Meeting of the Directing Council of PAHO of an item on the control and eradication of Aedes aegypti.

The document entitled, "Aedes aegypti/Flavivirus control and prevention," has been prepared in response to the above.

This document presents a historical background on the importance of tropical diseases, specifically dengue and yellow fever and their vectors.

A review of the resolutions adopted by the Directing Council and the Pan American Sanitary Conference since 1942 emphasizes the need for a regional policy to eliminate Aedes aegypti from the Hemisphere in order to prevent urban yellow fever and dengue transmission.

The epidemiological situation of dengue and yellow fever in the Americas and an analysis of the geographical distribution of those flaviviroses and of the vectors are discussed, as well as the problems in developing specific prevention and control programs.

Some areas for the strengthening of human resources capabilities and research also are mentioned, and a brief description of the role of PAHO is made with reference to technical cooperation and technical meetings.

Lastly, the document highlights the conclusions and recommendations made by the three PAHO Scientific Advisory Committees which have met since 1976.

Introduction

Urban yellow fever (UYF) and dengue fever (DF) represent a potentially serious problem in the Americas, and their distribution, recrudescence and transmission dynamics are related to the infestation level of the mosquito vector, Aedes aegypti.

Factors determining mortality and morbidity rates depend upon the vector capacity, the immune response and status of the population at risk and the type of strains of circulating virus in a given area.

The possibility of having outbreaks of DF, dengue haemorrhagic fever (DHF) and dengue shock syndrome (DSS) is increasing in most of the countries of Central America, Mexico and the Caribbean because of the high level of infestation by the vector. The fact that a large section of the population of these countries live in precarious social and economic conditions, the unsanitary conditions of the dwellings, and migrations due to political and economic reasons, all contribute to the risks of these disease entities.

In South American countries, besides DF, DHF and DSS there is also the possibility of UYF outbreaks, not only because of the heavy infestation with Aedes aegypti in certain urban areas but because the possible adaptation of this vector to rural conditions, and the "urbanization" of wild vectors of the genus Haemagogus.

The possibilities of mixed infections (UYF/DHF) is not remote if infestation indices of Aedes aegypti remain high.

These diseases are important not only from the point of view of the individual but also in terms of the health services which will be hard pressed to deal with epidemics. Although there is an excellent vaccine against YF, there may be serious production and logistical problem in providing it in case of a severe epidemic.

Historical Background

The Pan American Health Organization has been interested in tropical diseases and specifically YF since its inception. A review of the essential resolutions of the Governing Bodies points out clearly the importance of diseases transmitted by the vector <u>Aedes aegypti</u>.

During the 19th century, the United States of America suffered from repeated outbreaks of cholera imported from European immigrants and yellow fever transported by sea from Central and South American countries and Cuba.

In 1880, the United States Congress authorized the President to convene the Fifth International Sanitary Conference in Washington, D.C. for the purpose of setting up an international reporting system with respect to the sanitary situation in ports and localities. This decision stemmed from approval of a decree that included provisions falling outside the jurisdiction of the United States and that could only be enforced through an agreement with all the countries with which the United States had maritime relations. The decree testified to the almost continuous threat of importation into the United States by sea of yellow fever from countries of the South and of cholera from Europe.

In this Fifth Conference, held in February 1881 and attended for the first time by delegates from the Americas, a scientific hypothesis of major importance was publicly announced. The distinguished special delegate from Spain, Carlos Finlay, representing the Spanish colonies of Cuba and Puerto Rico, declared that an intermediary agent was necessary for yellow fever to be transmitted from one human to another. Shortly thereafter Aedes aegypti (then know as Stegomyia fasciata) was identified as the culprit.

By 1901 sufficient light had been shed on the etiology and modes of propagation of cholera, plague and yellow fever to make possible a rational approach to their control. Among the recommendations made by the Second International Conference of American States in Mexico City (October 1901) was one requesting the Governing Group of the International Union of American Republics (now the OAS) to convene representatives of health administration for the purpose of setting out sanitary covenants and regulations in order to minimize quarantine requirements for cholera, yellow fever, bubonic plague, smallpox and other serious outbreaks of "pestilential diseases."

The First International General Health Convention of American Republics was thus signed, later to become the Pan American Sanitary Conference.

Brazil started to register urban yellow fever deaths in 1930 and initiated immunization in 1937. The last case of UYF was registered in 1942 at Sena Madureira City in Acre, Brazil. The anti-mosquito Aedes aegypti campaigns were initiated in Brazil in 1923. During 1926-1940 it was demonstrated that vector control methods could eradicate the mosquito. In 1940 the National Service of Yellow Fever was organized under the auspicies of the Division of International Sanitation of the Rockefeller Foundation.

The XI Pan American Sanitary Conference (1942) requested the Governments of the countries in which <u>Aedes aegypti</u> was found to organize eradication projects based on the plans adopted in Brazil.

In October 1958 the XV Pan American Sanitary Conference declared that Bolivia, Brazil, Belize, The Canal Zone, Ecuador, French Guiana, Nicaragua, Panama, Paraguay, Peru and Uruguay were free of Aedes aegypti, and appealed to the other countries and territories that were still infected to intensify their anti-Aegypti activities.

Guatemala and Honduras were declared free of Aedes aegypti in 1959; El Salvador, in 1960; Chile and Costa Rica in 1961; Mexico in 1963 and Argentina in 1965.

The XVI Directing Council (1965) urged the Governments of the countries and territories still infested by <u>Aedes aegypti</u> to make every effort to eradicate the mosquito as soon as possible. This recommendation was repeated even more forcefully by the XVII Pan American Sanitary Conference in 1966.

In 1969 the XIX Directing Council requested the Director to sponsor an in-depth study of the strategy and methods of preventing the diseases transmitted by Aedes aegypti.

Between 1970 and 1980 the Governments were urged repeatedly by the Governing Bodies to organize or intensify activities for the epidemiological surveillance of diseases transmitted by Aedes aegypti without prejudice to the continuation of action for the eradication of the vector. They were encouraged to continue research on other mechanisms for the control of diseases transmitted by Aedes aegypti, including the development and testing of an effective vaccine against dengue, with due regard for methods currently being used against the vector.

In 1981 the XXVIII Meeting of the Directing Council requested the Director to organize a technical group comprised of representatives of the most severely affected countries to study the problem and propose possible alternative courses of regional action for the eradication of Aedes aegypti as well as other approaches to controlling dengue and dispelling the threat of urban yellow fever in the Hemisphere.

The Technical Group met and on the basis of its findings and recommendations, the XXI Pan American Sanitary Conference (1982) resolved, inter alia:

- To maintain the present policy for eradication of Aedes aegypti from the Hemisphere and to recommend to the Governments of the countries and territories still infested by the vector that

they take appropriate measures to remove the financial and administrative difficulties that may be hindering the progress of their programs, and that they give such priority as is necessary to the allocation of funds, personnel and materials for the completion of those programs.

- To recommend to each Government considering that the general goal of eradication will not be reached by all the countries in the Region in the short run, and in view of the danger of fresh dengue epidemics and the threat of urbanization of yellow fever, that it draw up an emergency plan to inventory the resources available in neighboring countries and a plan of operation for implementation in the event of an epidemic.

Epidemiology of Dengue in the Americas

Although epidemics of dengue-like fever have been reported in the Caribbean since 1827, the first documented pandemic occurred in the Region in 1963 and was caused by dengue type 3. Subsequently, up to 1977, a large number of dengue epidemics were confirmed in the Caribbean and in the northern part of South America, associated with dengue virus serotypes 2 and 3. It is estimated that in Colombia alone more than 650,000 persons were affected by the epidemics of 1971-1972 and 1976-1977 (Table 1).

In early 1977, an epidemic caused by dengue type 1 was reported in Jamaica and marked the beginning of a period of extreme activity of the virus in that year and in subsequent years. Virtually all the islands of the Caribbean were attacked by the virus. In South America, epidemics broke out in Colombia, French Guiana, and Venezuela, while in Middle America epidemics were reported in Honduras, El Salvador, Guatemala, and Belize. The epidemic spread to the northern part of the Hemisphere and reached Mexico in 1980; in the second half of that year, it even spread to the State of Texas in the United States of America, where some autochthonous cases were confirmed, a phenomenon that had not been observed since 1945.

About 702,000 cases of dengue were reported by the countries in those four years (1977-1980) in which dengue-1 was active, and although that figure is clearly an underestimate of the real incidence, it nevertheless demonstrates the magnitude of the epidemic.

In 1981 two important events in the history of dengue in Americas occurred: the introduction of the virus serotype 4 and occurrence of the first epidemic of hemorrhagic dengue fever in Americas. Fortunately, cases of dengue-4 have so far been benign and the limited outbreaks have been confined to the Caribbean islands of St. Bartholomew and St. Maarten, Puerto Rico, St. Thomas, Dominica and possibly Haiti and Jamaica. In 1981, Cuba was struck by a widespread epidemic of dengue-2, which affected more than 300,000 persons. classical benign febrile syndrome of dengue was accompanied by serious hemorrhagic manifestations and shock. A total of 150 fatal cases was reported, most in children under 15 years of age.

TABLE 1. REPORTED CASES OR SUSPECTED OUTBREAKS OF DENGUE IN THE CARIBBEAN AREA, 1972-1977

Country and other political unit	1972	1973	1974	1975	1976	1977 ^(a)
Antigua	_		_	_	-	4
Bahamas	-	-	-	-	-	934
Barbados	-	-	-	-	-	1
Bermuda	-	-	-	-	-	1
Colombia	P			P	P	Р
Cuba	• • •	-	-	-	• • •	477 438
Dominica	-	-	_	-	_	408
Dominican Republic	-	-				P
French Guiana			-	-		P 15
Grenada	-	• • •	1	-	-	15
Guatemala		-	-	6	-	4
Guyana	-	-	-	•	-	P
Haiti	3	103	441	351	99	238
Jamaica	4	3	2	1	5 2	9 911
Mexico Netherlands	-	-	• • •	-	2	
Antilles						P
Puerto Rico	85	710	44	1 214	a) 183	10 290
Trinidad and Tobago Turks and Caicos	-	-	• • •	-	-	6
Islands		30	20		a) 2	51
Venezuela (b)	25	Š	-	• • •	, <u>-</u>	
Virgin Islands (UK)	- 2	_	-	-	_	_
Virgin Islands (US)		-	-	-	,·· P	P

P Outbreak or presence of dengue-like illness reported.
(a) Provisional data.

Source: Health Conditions in the Americas (1973-1976), PAHO

⁽b) Reporting area.

The outbreak of DHF in Cuba added a new dimension to the problem of dengue in the Americas. Although its occurrence in this Hemisphere so far has been limited to Cuba, if we examine what happened to that disease in Asia, we see that following its appearance in the Philippines in 1953 it gradually spread to other countries of Southeast Asia, such as Thailand, Viet Nam, Malaysia and Singapore, as well as to Indonesia and other countries of the Western Pacific. The seriousness of the problem in Asia is shown by the fact that, up to 1978, 250,000 cases of DHF had been confirmed, with about 12,000 fatalities.

Tables 2 and 3 show data on the reported cases of dengue from 1977 to 1985 in some countries of the Americas.

TABLE 2. REPORTED	CASES	OF	DENGUE	ΤN	SELECTED	COONTETES,	13//-1301
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Country	1977	1978	1979	1980	1981
Colombia	•••	15,945	12,134	9,894	• • •
Cuba	477,440	75,694	1,497(a)	699(a)	344,203
El Salvador	• • •	16,869	23,146	1,651	5,170
Honduras	-	1,953	1,753	1,099	1,612
Jamaica	11,900	4	25	9	49
Trinidad and Tobago	8	343	38	-	15(4i)

Source: Health Conditions in the Americas (1977-1980), PAHO

(a) Provisional data. (i) Imported cases

After the relatively high level of dengue activity in the Region of the Americas in 1981 and 1982, most countries noted only low-level or sporadic transmission in 1983. However, Mexico, Colombia, and El Salvador--all of which experienced epidemics in 1982--had significant, localized outbreaks in 1983. Overall, 37,168 dengue cases were reported in the Region in 1983, compared with 50,450 in 1982 (Table 3).

TABLE 3. REPORTED CASES OF DENGUE 1981-1985

Country	1981	1982	1983	1984	1985*
Anguilla	-	-	2	_	_
Antigua	3	25	1	-	-
Barbados	6	99	63	63	_
Belize	7	482	26	127	17
Colombia	2,872	6,537	4,977	-	
Cuba	344,203	-	-	-	-
Dominica	17	-	2	-	
Dominican Republic	-	435	538	260	-
El Salvador	5,170	5,095	2,692	462	-
Grenada	2	7	6	3	-
Guadeloupe	-		_	339	44
Guatemala	96	33	2	-	_
Haiti	145	215	483	328	-
Honduras	1,612	1,217	729	378	10
Jamaica	49	21	26	12	_
Mexico	831	30,904	23,512	• • •	•••
Puerto Rico	493	9,536	2,836	1,750	• • •
St. Christopher-Nevis	10		-	-	1
Saint Lucia	8	31	-	-	_
St. Vincent	4	1	-	· ·,	-
Suriname	16	25	-	-	***
Trinidad and Tobago	15(4i)	16	122	30	
United States of America	2(i)	45	27	-	***

Source: PAHO (ADS)

^(*) Reported up to March 1985

⁽i) Imported cases

In Mexico, 23 of the 30 states reported 23,513 dengue cases in 1983, compared to the 30,904 cases notified by 17 states in 1982. It is estimated that dengue virus is circulating in less than 10% of that country, despite an increase in the number of affected states. Attack rates over 100 per 100,000 inhabitants were recorded in the states of Chiapas, Guerrero, Oaxaca, and Puebla, and the disease is apparently showing an ascendant trend in those states. For the first time the cities of Guaymas (in the northwestern state of Sonora), Guamúchil (in the neighboring state of Sinaloa), and Zihautanejo (in the south-central state of Guerrero) reported cases in 1983. Significant virus activity was detected in the cities of Tapachula and Tuxtla Guitérrez (Chiapas), Mérida (Yucatán), (Guerrero), and Veracruz (Veracruz). Laboratory surveillance showed that at least three dengue serotypes were circulating in the country in 1983. Dengue-4 was isolated from two persons in the state of Guerrero, and dengue-1 was recovered from the states of Puebla and Sonora.

Colombia reported 4,977 cases for the first six months of 1983. Two serotypes, dengue-1 and dengue-4, were isolated from patients sera in 1983, and both were probably responsible for some outbreaks. Additionally, serologic data obtained by the arbovirus laboratory--Instituto Nacional de Salud en Bogotá--suggest that dengue-2 and dengue-3 may still be transmitted in some areas of the country; if so, Colombia would be the first country in the Region to have simultaneous transmission of all four dengue serotypes.

In El Salvador, 3,814 cases were reported in 1983, compared with over 5,000 in 1982. An increase in the number of cases began in late June and early July 1983, in the capital, San Salvador, where dengue-4 was the isolated serotype. By late August, cases were reported from most areas of the country, but the largest outbreak occurred in the eastern region bordering Honduras.

Barbados, Haiti, Jamaica, and Trinidad experienced small dengue outbreaks in 1983. In Jamaica, dengue-2 predominated, although serologic evidence from U. S. travelers suggested that dengue-4 was still active as well. Dry weather was probably responsible for limited transmission. Haiti, the outbreak was apparently limited to the city of Belladere and the surrounding area on the border with the Dominican Republic. Dengue-1 virus was isolated, confirming earlier serologic evidence of serotype occurring among medical missionaries working in Haiti. Despite epidemic dengue activity in Haiti, relatively few cases were confirmed in the Dominican Republic in 1983. Dengue-4 activity remained high in Trinidad and Tobago throughout 1983, with peak transmissions from July October. This serotype was isolated by the Caribbean Epidemiology Center (CAREC) laboratory from 115 cases, compared with only four dengue-2 cases isolated in 1983. In Barbados, dengue-4 was active early in the year, but no isolations were made from April through September. Another virus isolate was made in October, but travel history on the patient was not available.

Following two consecutive years with major epidemics (dengue-1 in 1981 and dengue-4 in 1982), Puerto Rico experienced little confirmed dengue activity in 1983. Dengue-4 virus was isolated only once in 1983 (January), but serologic evidence confirmed sporadic transmission of that serotype throughout the year.

An overview of serotypes shows that dengue-4 was the predominant virus in the Region again in 1983, but dengue-1 also had a wide distribution (Figure 1). There was renewed activity of dengue 2 in the western part of the Region (Jamaica, Mexico): dengue-1 transmission was confirmed only in Colombia, Haiti, Honduras, and Mexico. However, all four types were introduced into the Region, as evidenced in the United States of America (Table 3, Figure 1).

Clinically, the Americas experienced classical dengue illness in 1983. There were apparently no cases of confirmed dengue hemorrhagic fever (DHF) in the Region. Health authorities in Colombia, however, reported several cases of fatal hemorrhagic disease that were not confirmed as either dengue or yellow fever. Confirmed cases of dengue associated with encephalitic signs were observed in the Dominican Republic.

Prior to 1981 only dengue serotypes 1, 2, and 3 were known to circulate in the Americas. In 1981, however, the presence of dengue-4 was documented in the Hemisphere for the first time. Dengue-4 infections were initially confirmed in two U.S. citizens who visited the island of St. Barthélemy, French Antilles, in March-April 1981. Both cases were serologically confirmed. Further investigations revealed that an outbreak of dengue occurred in St. Barthélemy during February-June. Dengue type 4 is known to be endemic in Southeast Asia and in the South Pacific. It remains unknown as to how the virus was introduced in St. Barthélemy, a small and relatively remote island in the Caribbean; however, it is possible that the island's links with French Polynesia may explain the appearance of the virus in the Caribbean.

Surveillance was intensified in the Caribbean and, as a result, outbreaks of dengue-like illness were known to have occurred in Curaçao, Dominica, Guadeloupe, and St. Martin. Dengue-4 activity in Dominica probably started in March of 1981, but laboratory studies were begun only in May. At least 59 strains of dengue-4 were isolated from Dominica residents. Four dengue-4 cases from St. Martin were reported in August 1981.

During the following months and in 1982, dengue-4 circulation was detected in other Caribbean islands and in Belize. Islands affected in the Caribbean included St. Thomas, Puerto Rico, Jamaica, Haiti, and Trinidad and Tobago. Laboratory evidence of infection was obtained from the indigenous population or from visitors to these islands. Dengue-4 isolates were also obtained from a few patients in Grenada and St. Kitts from August to October. It is not clear if these infections occurred in these islands or elsewhere.

FIGURE 1 - DENGUE IN THE AMERICAS, 1983.



Four cases of dengue-4 (three U.S. citizens and one Canadian) were documented serologically after travel to Haiti from July through September. A dengue-4 strain was also isolated from the Canadian patient.

In St. Thomas, 38 cases of dengue have been confirmed by hemagglutination-inhibition serologic testing and one case by virus isolation. The isolate was identified as dengue-4 and a serologic diagnosis of dengue-4 was made in another case. A total of 33 had onset of illness in August, and five in September.

Isolations of dengue types 2 and 4 were obtained from patients in Jamaica in the second half of 1981. Evidence of primary dengue type 4 infection was confirmed in five U.S. citizens who visited Jamaica in October and one who visited in February 1982.

Trinidad and Tobago reported six imported cases of dengue type 4 (from Curação, Dominica, Martinique, and Saint Lucia) occurring form June to October 1981. Three additional isolations of this virus and one of dengue-1 were obtained between March and May of 1982 from autochthonous cases.

Dengue-4 activity was sporadic in Puerto Rico from August to October 1981, a period during which the island was being affected by an outbreak of dengue type 1. In November and December, dengue-4 was the dominant virus isolated in Puerto Rico; at least 79 strains of dengue-4 were obtained in the island during 1981. During the first two months of 1982, reported dengue-4 activity was increasing again. A primary serologic response to dengue-4 has been obtained from a patient in Belize with onset of illness during July 1982. Dengue-4 infections were also documented in two U.S. citizens who visited Martinique in February 1982.

Circulation of dengue-4 virus in South America was reported in As of June 1982, 12 cases of dengue-4 infection of all age groups 1982. had confirmed in Suriname through virus isolation. seroconversions to flavivirus were also documented. Investigations undertaken in late March 1982 revealed that at least 10 per cent of the population of Paramaribo, Suriname, had suffered from a dengue-like illness since January 1982. Strains of serotypes 1 and 4 were isolated from several cases during an outbreak of dengue-like illness in Boa Vista, northern Brazil, during March-May 1982. Retrospective studies suggested that the outbreak may have started as early as October 1981.

Illness associated with dengue type 4 viral infection has been self-limited and generally mild, with no evidence of hemorrhagic fever. Virus activity has been low to moderate, and in spite of widening dissemination of the virus, it has not caused a widespread outbreak in the Hemisphere. Nevertheless, countries should reinforce their surveillance systems to detect the presence of the agent and implement control measures.

EPIDEMIOLOGY OF YELLOW FEVER IN THE AMERICAS

Yellow Fever in the Americas

In the period 1965-1979 the average annual number of cases of jungle yellow fever in the Americas, as reported to the Pan American Sanitary Bureau, was 114.

Since 1972, incidence of the disease has shown an upward trend with peaks occurring in two- or three-year cycles and gradually affecting areas in which no cases had previously been reported. The annual transmission cycle (according to data for 1975-1978) usually began in December-January, reached it peak in April-July, and declined to its lowest level in September-November.

In 1978 six countries--Bolivia, Brazil, Colombia, Ecuador, Peru, and Venezuela--reported cases of jungle yellow fever. This is the highest number of reporting countries in 25 years (see Table 4). As of year-end 1978 a total of 240 cases had been registered (provisional figures).

Trinidad and Tobago reported 18 cases of jungle yellow fever in 1979 and, following confirmation of the initial cases, about 85 per cent of the population was vaccinated against the disease.

In Colombia, an epidemic broke out in mid-1978, in the Tarra region in rural areas adjacent to forests; 28 deaths due to jungle yellow fever were reported, 13 of which were confirmed. Some of the patients were transferred for treatment to nearby urban communities that were infested by Aedes aegypti, where they subsequently died; no cases of the disease transmitted by that mosquito were confirmed, however. In 1979 Colombia reported 51 cases of jungle yellow fever in the Departments of Cesar (13), Magdalena (30), Meta (6), and Santander (2).

No data are available on the number of inhabitants exposed to jungle yellow fever or on the number of those vaccinated against the disease in the various countries.

In view of this situation, PAHO held a meeting of experts in yellow fever in Washington, D.C., in July 1979. The group concluded that, although the annual vaccine production in Latin America was 8 million doses—6 million prepared in the Oswaldo Cruz Foundation in Rio de Janeiro and 2 million in the National Institute of Health in Bogotá—the current stock was low (2.1 million doses in Rio de Janeiro and 400,000 doses in Bogotá) and insufficient to meet the demand in the event of an urban epidemic. The group recommended that 5-10 million doses be available at all times.

TABLE 4. REPORTED CASES OF YELLOW FEVER BY COUNTRY, 1950-1985

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Source: Baalth Conditions in the Americas: 1950-1953; June 1958; 1957-1960;1961-1962; 1961-1964, and 1965-1968.
Epidemiological Bulletin, Vol.1, N°1, 1980; Vol.4, N°1, 1983.
BEE files; 1983, 1984 and 1985 of cases reported by countries.

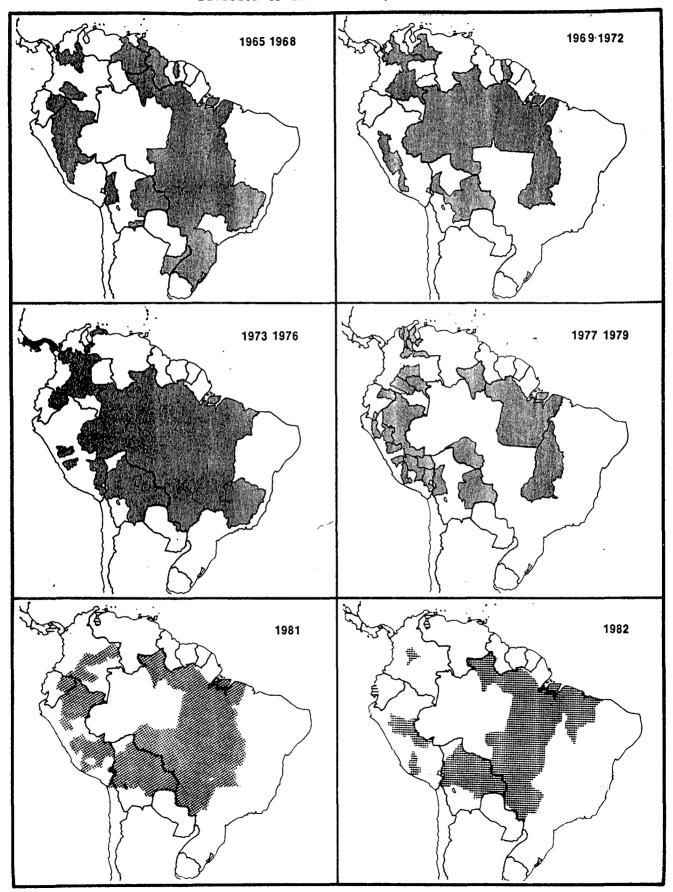
* provisional data ** up to June 30, 1985 The recommendation was also made that the surveillance systems in use at present be reviewed and that only persons exposed to risk be vaccinated. Although there is no evidence of a teratogenic effect of the 17D chick embryo vaccine, pregnant women should only be vaccinated if exposure to risk warrants it.

Five countries in the Americas reported cases of jungle yellow fever between 1981 and 1982 (Bolivia, Brazil, Colombia, Ecuador and Peru). A total of 368 cases were noted during this period, constituting a slightly higher incidence than was observed in the preceeding two years (315). Bolivia and Peru accounted for 84.8% (312) of the cases in 1981-1982, whereas Brazil reported 12.5% (46). Colombia reported 2.2% (8), and only two cases were detected in Ecuador. During 1981 there was an epidemic in Rincón del Tigre, a locality of Sandoval Province in the Department of Santa Cruz, Bolivia, which accounted for about 50% of the cases reported by Bolivia that year.

There was a total of 183 deaths reported during the biennium and, with a single exception, all survivors were reported from Bolivia and Peru. In Rincón del Tigre the case fatality ratio was about 10%, although diagnosis of the outbreak was retrospective and based mainly on clinical grounds. It should be noted that Brazil reports only confirmed yellow fever cases, whereas Bolivia reports all suspected cases in an endemic area. This variation in case reporting criteria constrains major analysis regarding case fatality ratios.

Figure 2 shows the areas in which endemic yellow fever cases were recorded in the Americas. With the exception of the 1981 outbreak in Rincón del Tigre, all cases reported in 1981 and 1982 occurred in known endemic areas of the disease. However, the last confirmed outbreak of yellow fever to occur in the Andrés Ibánez Province of the Department of Santa Cruz, Bolivia, was in the late 1940's, which illustrates the virus' potential to reappear after long intervals of quiescence. The 1980-1981 outbreak which involved the states of Goias, Mato Grosso, and Mato Grosso do Sul, on the other hand, demonstrates that the cyclical appearance of the virus continues to occur in central and western Brazil. confirmed outbreak in the state of Goais was in 1935 and was followed by others occurring at intervals of five to nine years. The assumption is that these epidemics reflect virus excursions from the enzootic areas of There has nevertheless been a decline in the the Amazon Region. incidence of the disease, which is the result, in part, of the intensification of vaccination programs throughout endemic areas, although it must be recognized that surveillance may not be adequate in In Brazil, for example, about three million doses of remote areas. vaccine are administered annually (3,300,000 in 1981), utilizing the 17D vaccine produced by the Oswaldo Cruz Foundation in Rio de Janeiro.

FIGURE 2. REPORTED CASES OF JUNGLE YELLOW FEVER BY MAJOR POLITICAL DIVISION OF EACH COUNTRY, 1965-1979*



Shaded areas indicate political divisions that reported cases of jungle yellow fever

* Up to 31 December 1979 (Pravisional Data)

The monthly distribution of cases in the biennium clearly indicates that the highest number of cases occurs in the first half of the year, peaking in March. This is probably due to the higher densities of <u>Haemagogus</u> mosquitoes (the main jungle yellow fever vectors in the Americas) during the rainy season. It is conceivable, however, that the outbreaks observed during the first months of the year may be associated with increased work in rural and forest areas carried out by susceptible populations in places where yellow fever is enzootic.

Sex and age distribution were known only for 347 cases. Males outnumbered females by a large proportion. A majority of the cases (79.3%) was between 15 and 34 years of age. No cases were recorded in those under one year of age and, except for one, all cases occurring in the 1-4 age group were documented in the Rincón del Tigre region during the 1981 epidemic. On the other hand, all Brazilian cases were over 15 years of age. This age and sex distribution of patients is consistent with patterns of jungle (transmitted) disease. No cases of urban yellow fever have been documented in the Americas for the past four decades in spite of the fact that several jungle cases have been hospitalized in Aedes aegypti infested towns during this period.

Vector Control in the Americas

The failure of control programs can be attributed to the following factors which operate to a greater or lesser extent in the countries which are infested or were free and have been reinfested:

- Lack of available data on vector biology and ecology which should form part of an epidemiological surveillance system with the sensitivity to respond promptly and to follow the application of the right methodology to local situations.
- Lack of staff trained in medical entomology and vector control who could contribute their knowledge to the epidemiological study of tropical disease and participate in the planning and execution of measures for interrupting the transmission cycle.
- The widespread resistance of vectors to insecticides, and the toxicity of insecticides to humans.
- Lack of coordinated programs for the reduction of contact between humans and vectors in community development projects and drinking and irrigation water supply projects.
- Shifting government priorities which prevent the commitment of budget or staff in quantities sufficient to ensure coverage of infested areas.

But the Aedes aegypti mosquito and the diseases it transmits and can transmit are still present in the Americas. The absence of any epidemic of urban yellow fever for several years running and the established effectiveness of 17D yellow fever vaccine has dispelled the fear that in the past was the chief incentive to the conduct of productive campaigns for the eradication of Aedes aegypti in practically almost all the countries of the Americas. Moreover, the emergency situation created by a dengue epidemic in most of the Caribbean countries since 1977-1978, which has had serious socioeconomic effects, and the hemorrhagic dengue cases that occurred in Cuba in 1981 have aroused renewed interest in strengthening programs for the control or eradication of Aedes aegypti.

In the technical sense there is no obstacle to eradication of the mosquito. Growing progress in insecticide technology, the availability of high-performance equipment requiring little manpower to use and the introduction of new methods represent resources which, properly used, could eliminate Aedes aegypti.

The current distribution of the <u>Aedes</u> <u>aegypti</u> mosquito in the Americas poses a public health problem to the countries in the northern part of South America (Brazil included), the Caribbean islands, mainland Mesoamerica, Mexico and the southeastern United States of America. In some of these countries, the level of infestation is stable, while others are vector-free or have suffered low-density infestations.

Argentina, Chile, Uruguay, Panama, and, lately, Costa Rica, have reported themselves free of <u>Aedes aegypti</u>. Having eliminated localized reinfestations, Ecuador, the Cayman Islands, Saba and St. Eustatius are also vector-free and in the consolidation phase. Cuba is in the final stages of its program to eradicate Aedes aegypti.

However effective surveillance systems must be maintained even in the countries which are free of the vector, because the wide geographical distribution makes reinfestation always a possibility.

In many countries, control has been focused entirely on the provision of insecticides and their proper use, but the sociological aspects connected with control of $\underline{\text{Aedes}}$ $\underline{\text{aegypti}}$ are of demonstrated importance, as was the case in Cuba.

The aspects connected with the characteristics of the population, its habits, customs and traditions show that, without the participation of the organized community, neither control nor eradication can be achieved in densely populated areas. Equal importance is given to the way in which health education activities are carried out at the onset of an epidemic as well as during eradication. The incentives given to residents who participate in environmental sanitation activities, and competitive programs established by campaign workers, are of paramount importance as well.

TABLE 5. \underline{AEDES} $\underline{AEGYPTI}$ INFESTATION IN THE AMERICAS AREA IN KM²

Country or Other Political Unit	Total	Area Initially Infested	% of Total Area	Actual Situation	Activity in Progres
Antigua, Barbuda and Redonda	442	280	63.3	Infested	+
Argentina	2,779,741	1,000,000	36.0	Eradic. completed	v
Aruba	190	174	91.6	Reinfested	+
Bahamas	11,405	11,405	100.0	Infested	+
Barbados	430	171	39.8	Infested	+
Belize	22,965	22,965	100.0	Reinfested	+
Bermuda	53	· 53	100.0	Negative	v
Bolivia	1,098,581	100,000	9.1	Reinfested	+
Bonaire	281	246	87.5	Reinfested	+
Brazil	8,511,965	5,358,822	63.0	Reinfested	+
Colombia	1,138,338	280,000	24.6	Infested	+
Costa Rica	50,700	20,000	39.4	Reinfested	+
Cuba	114,542	100,000	87.3	Infested (almost negative)	+
Curação	472	448	94.9	Infested	?
Chile	756,945	100,000	13.2	Eradic. completed	v
Dominica	789	789	100.0	Infested	+
Ecuador	283,561	69,454	24.5	Erad. completed	v
El Salvador	21,393	18,675	87.3	Infested	<u>-</u>
United States of America	9,359,781	1,536,819	16.4	Infested	_
Grenada-Grenadines (Carriacou, Petit Martinique		,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,			
and Union)	344	344	100.00	Infested	+
Guadalupe (and part of					
St. Martin	1,779	1,619	91.0	Infested	?
Guatemala	108,889	36,423	33.4	Reinfested	+
French Guyana	91,000	91,000	100.0	Reinfested	+
Guyana	214,969	4,662	2.2	Infested	+
Haiti	27,750	27,750	100.0	Infested	_
Honduras	112,088	69,929	62.4	Reinfested	+
Caiman Islands	259	259	100.0	No information	?
Turks and Caicos Islands	430	430	100.0	Infested	?
JS Virgin Islands	344	344	100.0	Infested	?
British Virgin Islands	153	153	100.0	Infested	+
Jamaica	11,424	11,424	100.0	Infested	+
Martinique	1,102	1,000	90.7	Infested	?
1exico	1,972,546	1,000,000	50.7	Reinfested	+
iontserrat	103	103	100.0	Infested	+
Nicaragua	130,000	65,263	50.2	Reinfested	+
Panama	75,650	56,246	74.3	Negative	v
Paraguay	406,752	200,000	49.2	Reinfested	+
Peru	1,285,215	638,000	49.6	Reinfested	+
Puerto Rico	8,896	8,896	100.0	Infested	+
Oominican Republic	48,734	42,020	86.2	Infested	+
Saba, St. Eustatius	29	29 -	100.0	Reinfested	+
St. Christopher-Nevis-Anguilla	396	396	100.0	Infested	+
St. Martin (Dutch part)	60	60	100.0	Infested	+
St. Vincent	388	332	85.6	Infested	+
Saint Lucia	616	259	42.0	Infested	+
Suriname	142,822	48,000	33.6	Infested	+
Trinidad and Tobago	5,128	3,108	60.6	Infested	+
Jruguay	186,926	186,926	100.0	Eradic. completed	v
/enezuela	912,050	710,000	77.8	Infested	+

^{+:} Activity -: No activity v: Surveillance ?: No information

THE ROLE OF PAHO

Technical Cooperation

The Pan American Health Organization has cooperated with the Member Countries in the coordination of surveillance, control, and research.

Surveillance activities benefit from the network of laboratories situated in Colombia, Cuba, French Guiana, Jamaica, Panama, Puerto Rico, and Trinidad and Tobago and the assistance of the Regional Dengue Reference Center of the United States Army Walter Reed Institute (WRAIR). The Walter Reed Institute and the U. S. Centers for Disease Control (CDC) have supplied a number of laboratories with reagents including the recently-developed monoclonal antibodies. Several workshops on the laboratory diagnosis of dengue have been held under the coordination of PAHO and with the cooperation of the Walter Reed Institute and the CDC, and manuals on the diagnosis of the virus have been prepared.

Epidemiological information is systematically distributed through the PAHO <u>Epidemiological Bulletin</u>, the <u>Bulletin</u> of the Caribbean Epidemiological Center (CAREC), as well as by telegraphic communications sent to all the countries to keep them informed of the behavior of the disease. PAHO has also provided several countries with epidemiological consultancies.

PAHO has assisted countries in organizing national programs for eradication of <u>Aedes aegypti</u>, in preparing emergency plans, and in obtaining insecticides, equipment, and materials. The preparation of an inventory of the resources available in the Caribbean for emergency vector control operations is an important contribution to the system.

The Organization has promoted research on: 1) ecology and biology of Aedes aegypti and the factors that help increase its distribution or reinfestation in areas previously free of Aedes aegypti; 2) evaluation of equipment, insecticides and procedures for applying them, for the purpose of improving control operations; and 3) surveillance of the potential for the spread of insecticide resistance in areas exposed to the risk of dengue and urban yellow fever. It has also cooperated in training entomologists and conducted courses on the utilization of modern insecticides, and other control methodologies.

Measures have been taken to ensure that the collection and maintenance of representative strains of yellow fever virus is handled at a single institution, the WHO Collaborating Center at Yale University in New Haven, Connecticut. PAHO has continued to encourage and support ecological studies on yellow fever in areas such as Brazil and Trinidad, where outbreaks occur periodically, and to determine whether the virus persists in these areas during inter-epidemic periods.

Technical Meetings

In the past 10 years important technical meetings have been held to examine the problems of yellow fever, dengue and the control of Aedes aegypti:

- a) First Meeting of the Scientific Advisory Committee on Dengue, Yellow Fever and Aedes aegypti. Panama 1976;
- b) Meeting of Experts on Yellow Fever. USA, 1979;
- c) Second Meeting of the Scientific Advisory Committee on Dengue, Yellow Fever and Aedes aegypti. Brazil 1980;
- d) Symposium on Yellow Fever. Brazil, 1980;
- e) Meeting of the Technical Group on Aedes aegypti, Dengue and Yellow Fever. Mexico 1982;
- f) Traveling Seminar on Dengue Hemmorragic Fever and Dengue Shock Syndrome. Colombia 1984;
- g) Meeting to Develop Guidelines and Protocols for Production of Yellow Fever Vaccine in Cell Cultures. USA, 1984;
- h) Seminar on Dengue Hemorrhagic Fever. Mexico 1985;
- i) First International Seminar on Dengue Hemorrhagic Fever in the American Region. Puerto Rico, 1985;
- j) Third Meeting of the Scientific Advisory Committee on Dengue, Yellow Fever and Aedes aegypti. Puerto Rico, 1985.

In Belem, Brazil, 18-22 April 1980, attention was drawn to a number of aspects of research—some well known, others more recent—which should be taken into account in the Americas. These include studies of competition between various Aedes aegypti vector strains in transmitting yellow fever virus; genetic and transovarial transmission of yellow fever in Aedes mosquitoes; use of insect cell lines (in cases in which mice cannot be used for isolation of the virus), in diagnosing yellow fever, and possibly as a substrate for production of vaccine; and duration of antibodies in persons vaccinated.

Other new and promising aspects of research include use of the enzyme-linked immunosorbent assay (ELISA) test for serodiagnosis, development of radioimmunoassay and immunoassay tests in thin layer for detection of antigens, use of hybridomas for producing specific antibodies in vitro, and studies of interferon and other antiviral drugs in clinical treatment of the disease.

Other tests that should be compared with those currently in use include tests for plaque reduction neutralization, fluorescent focinhibition neutralization, and histopathology of the liver.

At the regional level, work has continued to ensure the prompt dissemination of information to Member Countries on the occurrence and distribution of any suspected and/or confirmed cases of yellow fever and DHF.

The participants of the Meeting of the Technical Group on Aedes aegypti, Dengue, and Yellow Fever (Mérida, Yucatán, Mexico, June 1982) also recommended increasing 17D vaccine production in Brazil and Colombia in order to meet rising demands; PAHO is helping these countries to modernize their production methods and seeks funds from international agencies to support the development of a 17D vaccine in cell cultures.

The III PAHO Scientific Advisory Committee (SAC) on Dengue, Yellow Fever and Aedes aegypti met on 17-18 June 1985 in San Juan, Puerto Rico, and evaluated the status of recommendations made by the SAC II in 1980.

Progress made in the modernization of yellow fever vaccines in Brazil and Colombia was discussed in detail, as well as the current situation regarding the inventory of isolated strains. The report of a seminar on treatment and laboratory diagnosis of yellow fever and the ecological studies on yellow fever were examined. The Committee also reviewed the vector biology in relation to emergency control.

After the review of the report of the Technical Group Meeting on Aedes aegypti, Dengue and Yellow Fever in Mérida, Mexico, in 1982, the situation of the third edition of the Guide for Diagnosis, Treatment and Control of DEF was also analyzed. Reports were made on the state of the art of the new developments in rapid techniques for the diagnosis of dengue and yellow fever, and how to upgrade dengue laboratories in the region. Reports on the epidemiological situation of DF, DHF and YF in Aruba, Brazil, Colombia, Mexico, Venezuela and the Caribbean countries were also discussed.

The SAC concluded that the epidemiology of yellow fever and dengue in endemic and epidemic zones of the New World is incompletely understood. Basic studies of interaction among viruses, vectors, and hosts are needed to improve ability to intervene in the cycles and to control the diseases. The rapid advances in molecular technology for detection of viral antigen and RNA, and in vector genetics, offer refinements applicable in field epidemiological studies.

The Committee recommended that attention be paid to the use of recently developed sensitive and specific techniques for early diagnosis that could be applied in laboratories without expensive equipment. Research is also required on new techniques, including detection of antigen by monoclonal antibodies or viral genome by nucleic acid hibridization.

Emphasis should be given in the short term to developing more effective surveillance, prevention and control measures. Those countries which have already eradicated or may eradicate Aedes aegypti should be encouraged to maintain eradication, and those countries which cannot achieve eradication should assume the responsibility of preventing the exportation of Aedes aegypti.

It was recognized that training of personnel can best be accomplished by utilization of centers of excellence for areas such as epidemiology, entomology, diagnosis, surveillance, molecular technology, and clinical management. The Committee finally recommended a close liaison between PAHO and funding agencies to integrate programs in research and training in DF, YF and Aedes aegypti.