PAN AMERICAN HEALTH ORGANIZATION

WORLD HEALTH ORGANIZATION

XXI PAN AMERICAN SANITARY CONFERENCE

XXXIV REGIONAL COMMITTEE MEETING

WASHINGTON, D.C.

SEPTEMBER 1982

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STUDY OF THE *AEDES AEGYPTI* PROBLEM

Corrigendum

Please make the following corrections on page 29:

- first paragraph, first line, and second paragraph, first line, substitute "yellow fever" for "malaria."

- fifth paragraph, eighth line, substitute "sloths" for "snakes."

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Item 18 of the Provisional Agenda

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STUDY OF THE AEDES AEGYPTI PROBLEM

At its XXVIII Meeting, held in September-October 1981, the Directing Council approved Resolution XXI, which requested the Director to organize a technical group to study the problem and propose possible alternative causes of regional action for eradicating Aedes aegypti and other approaches for controlling dengue and dispelling the threat of urban yellow fever in the Hemisphere.

In compliance with the above-mentioned resolution, the Director convened a meeting of a Technical Group in Merida, Yucatán, Mexico, from 1-5 June 1982. It was attended by 50 representatives of the most affected countries, PAHO consultants, and invited experts.

The Group noted that there had been a deterioration in the dengue situation in the Americas and that an increase in the activity of the virus in many countries had been confirmed, as had the introduction of new types such as type 1 and type 4; the appearance of hemorrhagic dengue fever (DHF) (Cuba, 1981); and the spread of dengue to new territories. Reports had been received of episodes of jungle yellow fever in 10 countries in the Region (in 1971-1981). In 1982 (up to 26 July), 117 cases had been reported, with 58 deaths in 3 countries in South America.

Preventing the urbanization of yellow fever at present calls for a combination of epidemiological surveillance measures, the vaccination of the human groups at risk, and the control of Aedes aegypti, the vector of urban yellow fever.

The Group emphasized the role played by Aedes aegypti control or eradication in the prevention and control of dengue as well as in the prevention of the urbanization of jungle yellow fever. In this last-mentioned regard, the Group concluded that it was technically feasible to eradicate Aedes aegypti, but factors impeding the achievement of this objective existed at the regional level. A dengue vaccine was likely to be available in the future but not for 5-8 years.

This report presents the recommendations of the Technical Group on epidemiological surveillance and disease prevention as well as on the diagnosis and clinical management of cases, the mobilization of resources in the event of epidemics, and research.

CSP21/22 (Eng.)

FINAL REPORT

MEETING OF THE TECHNICAL GROUP ON *AEDES AEGYPTI*, DENGUE AND YELLOW FEVER

Mérida, Yucatán, Mexico
1-5 June 1982

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I. CONDUCT OF THE MEETING

The Meeting of the Technical Group on Aedes aegypti, Dengue and Yellow Fever, convened in compliance with Resolution XXI of the XXVIII Meeting of the Directing Council of PAHO/WHO (Annex I), was held in Mérida, Yucatán, Mexico, from 1-5 June 1982.

It was attended by delegations composed of invited experts and representatives from the countries and territories particularly affected (Antigua, Bolivia, Brazil, Colombia, Cuba, French Guiana, Grand Cayman, Guatemala, Honduras, Jamaica, Martinique, Mexico, Nicaragua, Panama, Paraguay, Trinidad and Tobago, the United States of America, and Venezuela), as well as PAHO/WHO staff members and consultants from the Headquarters in Geneva, Washington, and the countries.

The Chairman of the inaugural session was Dr. Ramón Alvarez Gutiérrez, representing the Secretary for Health and Welfare of Mexico, and that of the closing session, Dr. Luis Cabrera Coello of the Secretariat for Health and Welfare.

Dr. Eduardo Zorrilla of Mexico served as General Rapporteur.

Inaugural Session

The inaugural session was held on 1 June 1982 and was attended by Dr. Luis Barceló Novelo, Secretary of Health for the State of Yucatán, representing the Constitutional Governor of the State, Major General Graciliano Alpuche Pinzón; Dr. Ramón Alvarez Gutiérrez, Chief, Unit of International Affairs, Secretariat of Health and Welfare of Mexico, representing the Secretary, Dr. Mario Calles López Negrete; the Director of the Pan American Sanitary Bureau, Dr. Héctor R. Acuña; Dr. Jorge Fernández de Castro, Director General of Epidemiology of the SSA of Mexico; Dr. Elsa Moreno, Representative of Area II of the Pan American Sanitary Bureau; and Dr. José Ojeda Ortiz, Chief of the Coordinated Health Services for the State of Yucatán.

Speaking on behalf of the Secretary of Health of Mexico, Dr. Ramón Alvarez Gutiérrez welcomed the participants and wished them every success in their endeavors.

Dr. Héctor R. Acuña explained to the members of the Technical Group that the objective to be achieved was to comply with the mandate of the Member Countries of the Organization, agreed upon at the XXVIII Meeting of the Directing Council, that the situation of the Aedes aegypti problem should be studied and possible alternatives should be proposed for eradicating the vector, controlling dengue, and preventing the urbanization of jungle yellow fever.

Dr. Luis Barceló Novelo, on behalf of the Governor of the State of Yucatán, delivered the inaugural address to the meeting of the Technical Group on Aedes aegypti, dengue and yellow fever, after which the inaugural session adjourned.

Agenda

At the meeting, presentation were made on six general topics:

i) General situation
ii) The Vector
iii) The Human Host
iv) The Virus
v) The Disease
vi) Comprehensive approach for obtaining better control of the problem

Recomendations and Conclusions

Following the presentation, the participants were divided into two groups, which drafted separate conclusions. The conclusions were submitted to the plenary session where they were approved and became recommendations of the Technical Group on the following:

- The Vector
- Epidemiological Surveillance
- The Vaccine
- Research

Inaugural Address, Dr. Héctor R. Acuña

On behalf of the Pan American Health Organization,* I have the honor to participate in the inaugural session of the meeting of the Technical Group on A. aegypti, dengue, and yellow fever. I should like to express my thanks for this opportunity that has been afforded us to one again enjoy the hospitality of this beautiful city of Merida, the capital of the State of Yucatán.

This meeting is of signal importance since there is no doubt that, among the infectious diseases that affect the population of the Americas, dengue fever and yellow fever are major public health problems.

In terms of morbility, dengue has a strong impact of the Region, especially in epidemic periods when hundreds of thousands of persons are affected by the disease. The harm caused by loss of employment, medical treatment, as well as the decrease in tourism in certain areas, amounts to hundreds of millions of dollars.

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* Pan American Health Organization, Pan American Sanitary Bureau, Regional Office of the World Health Organization.

The sharp increase in the incidence of jungle yellow fever in the certain countries of the Region, and the occurrence of outbreaks very near urban areas infested with A. aegypti, which involves the risk of the urbanization of the virus, are a matter of major concern.

Until recently, dengue fever appeared in the Hemisphere in a relatively benign form and only in exceptional circumstances were fatal cases associated with dengue reported. This situation began to change in 1981 when the first epidemic of hemorrhagic dengue fever (DHF) occurred in the Region and produced more than 150 fatal cases. Accordingly, the problem has become very important.

An historical approach to the problem of dengue in the Region clearly shows that it has increased considerably in the past two decades. Thus, 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 1971-72 and 1976-77.

In early 1977, the beginning of 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. Spreading to the northern part of the Hemisphere, the epidemic reached Mexico in 1980 and, in the second half of that year, even spread to the State of Texas in the United States of America, where some authochtonous 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 and underestimated of the real incidence, it nevertheless demonstrates the magnitude of the epidemic.

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

The outbreak of DHF in Cuba a new dimension to the problem of dengue in the Americas. Although its occurrence in this Hemisphere has so far 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, 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 fatal cases of DHF had been confirmed, of which about 12,000 were fatal.

The activities of the Pan American Health Organization in dealing with the dengue problem include the coordination of surveillance, control, and research.

Of major importance for surveillance activities is the role of 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 Center for Disease Control have supplied a number of laboratories with antigens 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 Epidemiological Bulletin, the Bulletin 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. It should be pointed out that PAHO has provided several countries with epidemiological consultancies either through its headquarters or through CAREC.

The Organization has provided the countries with technical and material assistance in their struggle against A. aegypti. This assistance is provided both in organizing national eradication programs and in preparing emergency plans. PAHO has also cooperated with the countries in obtaining insecticides, equipment, and materials. The cooperation provided also extends to the system of epidemiological surveillance and to the evaluation of A. aegypti control or eradication programs. 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 carried out studies on: 1) Ecology and biology of A. aegypti and the factors that help increase its distribution or reinfestation in areas previously free of A. 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, etc.

Despite the progress achieved by several countries in A. aegypti eradication or control programs, the infestation indexes continue to be very high in many others. Financial and social difficulties, in addition to operational difficulties and vectors resistance to insecticides, are some of the constraints on the success of the programs, as is the lack of a political decision.

In view of this situation, and the emergence of DHF in the Americas and the risk of the urbanization of yellow fever, the XXVIII Meeting of the Directing Council in Resolution XXI adopted on 30 September 1981 requested the Director of the Pan American Health Organization to convene a meeting of a group of experts that would include participants from the affected countries to study the problem and proposed possible alternative courses of regional action for eradicating A. aegypti and other means of controlling dengue and dispelling the threat of the urbanization of yellow fever.

Distinguished members of the Technical Group, the time has come to make an evaluation of the present status of the problem, with a new approach and perhaps new strategies. Let us very carefully examine the store of knowledge and resources available for dealing with that disease as well as other diseases transmitted by the vector. Let us consider the limitations of each one of them and let us formulate balanced and practical recommendations that may be universally adopted and applied to achieve the common objective of controlling dengue, yellow fever, and the vector that spreads them.

In this way we shall be participating in the great endeavor to achieve the goal of "Health for All by the Year 2000", by implementing the regional strategies of the Plan of Action to be adopted by the Member Countries of the Pan American Health Organization.

General situation of dengue, yellow fever and A. aegypti

Dr. Jaime Ayalde opened the discussion by referring to the status of dengue, yellow fever and A. aegypti in the Americas. He pointed out that since 1965 cases of jungle yellow fever had been reported in 12 countries in the Region of the Americas and drew attention to the fact that some outbreaks had occurred in places near urban areas infested by A. aegypti. The advance of human groups into jungle areas has favored contact with the reservoirs and vectors of the disease. The receptive urban areas must be identified and efficient systems of surveillance that permit the application of preventive measures, as well as the vaccination of high-risk individuals and A. aegypti control, must be implemented.

With respect to dengue, Dr. Ayalde pointed out that up to 1977 only serotypes 2 and 3 were known in the Region of the Americas. Dengue-1 was identified in the period 1976-1977 and dengue-4, in 1981. At the present time serotypes 1 and 2 are still active. As a rule, the disease has affected islands and coastal regions, but occasionally epidemics have occurred in regions geographically very distant from the coasts.

In June 1981, a dengue epidemic broke out in Cuba and cases presented the characteristics of hemorrhagic fever and the shock syndrome. Approximately 350,000 cases were reported during the epidemic, which ended in October of that year. About 10,000 cases presented serious manifestation and there were 158 deaths. Dr. Ayalde stated that this epidemic was the first occurrence of hemorrhagic dengue in the hemisphere.

With respect to A. aegypti, the mosquito had probable been present in the Americas since the end of the fiteenth century and had prompted the first example of cooperation of all the nations of the region to find a permanent solution to a common problem. In 1974 the Directing Council entrusted PAHO with solving the hemispheric problem of the urban yellow fever, basically through the eradication of the vector. Despite the present situation, the countries in which eradication is maintained are few and far between.

Dr. Paul Bres reviewed the status of dengue in the rest of the world and in particular in the endemic countries in four regions: Southeast Asia, the islands of the South Pacific, Africa and the Mediterranean. In the first of these areas, DHF was first described in 1956 in the Philippines, from where it had spread to almost all the countries of the region including Thailand, Indonesia, Burma, Malaysia, Singapore and Viet Nam, among others. Two main epidemic waves were recognized: the first in 1958-1965 and the second from 1970 to date. In these outbreaks all the dengue serotypes had been isolated.

In the islands of the South Pacific, dengue had occurred in two epidemic waves. The first in the 1940s, and the second, which began in the 1960s and still persists. The last-mentioned epidemic was the result of short sequential waves produced by serotypes 3, 2, 1 and 4. In this region DHF had been rather rare and had been found in adults; cases of primary infection due to each one of the serotypes had been confirmed.

The situation in Africa shows that at present there is no dengue epidemic activity. However, the systematic study of children with fever of unknown origin in Nigeria in 1966-1970 made it possible to isolate dengue virus type 1 and 2. In addition, in 1979-1981, dengue 2 was isolated from mosquitoes in West Africa, even in localities 1,400 meters above sea level and dengue virus type 2 was isolated from a monkey in Senegal.

Although an epidemic including hemorrhagic cases occurred in Greece in 1927-1928, the Mediterranean had been free of the disease since them.

With respect to yellow fever, WHO is of the opinion that the endemic area in Africa lies between parallels between 15°N and 10°S. The most important recent outbreaks occurred in Ghana and in Gambia.

With respect to the A. aegypti situation in the rest of the world, Dr. Normal Gratz commented that this mosquito was the most cosmopolitan of all the tropical species and was characterized by its great adaptability and plasticity. It probably originated in Africa where it reproduced in natural bodies of fresh water but easily adapted to artificial receptacles devised by man. This adaptability enabled it to spread widely to the entire African continent souch of the Sahara. It succeeded in heavily infesting the countries of the Mediterranean Basin where it became an efficient vector of dengue. At present there are some foci in Italy and Greece and probably in Turkey; it has reappeared in Israel; and is present on the Egyptian Coast of the Red Sea.

The man-made receptables transported by ships have enabled it to spead eastwards (Islands of the Indian Ocean, India, Sri Lanka, Bangladesh, Birma, Thailand, Indochinese Peninsula, coast of China on the western Pacific, and perhaps the south of Japan) and westwards, to the American hemisphere, and it has even been found in the past in points as far north as Philadelphia.

There was no doubt that A. aegypti continued to spread, even invading rural areas in some places; at present its outstanding characteristic is its ability to adapt to contemporary ecological changes, many of which are favorable to it, such as the inadequate disposal of waste, which provides it with potential breeding grounds.

II. THE VECTOR

Moderator: Dr. P. L. Tauil
Rapporteur: Dr. N. G. Gratz

Geographical distribution

Three participants dealt with the geographical distribution, biology, and egg-laying sites of A. aegypti in the Region. Dr. Michael Nelson dealt with the experience in South America. He stated that despite the fact that 9 countries had succeeded in eradicating the vector in the past, at present only Argentina, Chile, Ecuador, Peru and Uruguay were still free of A. aegypti. Bolivia, Brazil, Colombia and Paraguay eradicated the vector but had been reinfested while Venezuela, Guyana, Suriname and French Guiana had never eradicated the mosquito.

In the past, the infested sites had been at maximum altitutes of around 1,200 meters, but recently the mosquito had been found in Colombia at an altitutde of 2,200 meters, in a site at which the average temperature was 17°C, despite the fact that it has been demonstrated that it required an incubation period of at least 10 days at 18°C for the transmission of dengue to occur. Therefore the epidemiological importance of the presence of A. aegypti at sites higher and colder than usual remains to be demonstrated.

Dr. Michael Nelson also dealt with the penetration of A. aegypti into rural areas in Colombia. In the areas of South America he had studied, the most important breeding grounds are the relatively large man-made water receptables (high and low storage tanks and barrels) and also automobile tires. He noted that the smaller receptables were the least productive. Occasionally, breeding places were found in peridomiciliary sites in which rainwater accumulated such as hollows in trees, the high part of electricity poles, and others, but usually they were unproductive.

With respect to the Caribbean Region, Dr. Bruce Knudsen stated that Bermuda, the Cayman Islands and Tobago were the only three countries out of the 24 in the area that were still free of A. aegypti. In that area, the breeding places of the mosquito are found in hollows of trees, coconut shells, leaves, holes in coral, bamboo stakes, and man-made receptables of all types and sizes. However, the most frequent egg-laying habitat were barrels and cisterns, although in some sites the mosquito had shifted its preferred egg-laying site to roof gutters.

Dr. Donald Eliason described some aspects of the presence of A. aegypti in Middle America. He pointed out that in Mexico there were important diferences in the relative abundance of the vector that were related to the seasons and that these differences were more noteworthy in the northern part of the country, where the mosquito population decreased markedly during the winter because of the fall in temperature and the rainfall. Such variations were also noted in the south, although the were less pronounced. In Mexico the most important breeding places were tubs, tires, barrels, tanks, and laundries. He presented studies that showed the limitations of the usual infestation indexes due to their seasonal variations and proposed the use of indexes that took into account the surface on which the breeding places were distributed. He pointed out that the Breteau index entailed various degrees of infestation depending on the size of the houses studied and stated that the number of receptables with larvae and the number of discarded tires per hectare were indexes that proved to have significant correlations with the percentage of individuals that show dengue antibodies. He suggested that these indexes might be useful in predicting which were high-risk areas and consequently in planning preventive measures.

Finally he commented that the great variety of breeding places in the Region indicated that A. aegypti could adapt to a great variety of conditions for the purpose of reproduction. He noted the lack of sufficient studies on the habits of the adult mosquito and their relation to the transmission of diseases.

Genetic Aspects

Dr. Duane Gubler stated that the intrinsic ability of A. aegypti to adapt and its competence as a vector have a genetic base. The variation in vector competence may be of epidemiological importance and can explain patterns of geographical distribution and differences in the intensity of the transmission of a pathogenic agent of certain endemic and epidemic human diseases. Since vector competence has a genetic base, knowledge of it can be used to control diseases. Research on A. aegypti has been related to dengue virus and yellow fever virus. The factor that control the susceptibility of A. aegypti to oral infection with dengue virus are apparently the same for the four serotypes, and there is no doubt that this variation is controlled genetically. Similar variations have also been demontrated in the susceptibility of A. aegypti to oral infection with the yellow fever virus. In the case of dengue, the susceptibility is associated with an intestinal barrier; in the case of yellow fever, there may also be a barrier at the level of the salivary glands.

Dr. Gubler also reported on the results of his studies on the susceptibility of A. aegypti population in the south of the United States of America and the Caribbean to oral infection with the Mexican strain of dengue virus type 1. In general, A. aegypti from the coast of the Gulf of Mexico showed low indexes of infection. In contrast, the Caribbean strains showed greater susceptibility, especially a strain of A. aegypti from Villalba, Puerto Rico, where continuous transmission of dengue had existed for several years. A strain from Monte Morelos, Mexico, had a low infection index despite the fact that an outbreak occurred in 1980. The Caribbean strains also showed higher susceptibility in studies made with virus type 2.

Susceptibility studies were made on subpopulations of A. aegypti obtained from various districts of large cities in the United States of America. Marked differences were not found within each city, but the mosquitos from San Antonio, Texas; New Orleans, Louisiana; and Miami, Florida were much more susceptible to the infection with dengue virus than mosquitoes from Brownsville, Texas, and Corpus Christi, Texas. Other similar data suggests that the A. aegypti from Texas, Mexico, and El Salvador have low susceptibility while the Caribbean strains are more susceptible.

Since the variation in susceptiblity is a matter of genetic control, the genetic variation between populations of mosquitoes was studied by means of gel electrophoresis. These studies suggest genetic affinities between the strains of A. aegypti from Puerto Rico and Florida, and between the strains from New Orleans, Brownsville and El Salvador.

Dr. Gubler pointed out that other studied had provided comparable data on the susceptibility of A. aegypti to infection with yellow fever virus. Preliminary data suggest that the A. aegypti strains from the

Caribbean are more suceptible to oral infection with the Dakar strain of the yellow fever virus while the African strains of the vector are more resistant. It had also been reported that the Texas and Mexico strains were less susceptible to the virus while a strain from Trinidad was one of the most susceptible.

The genetic differences and the variation in susceptibility of A. aegypti to infection with flavivirus may be a factor that perhaps helps to explain the pattern followed by the dengue epidemics observed in the Region in recent years.

Control and Eradication Program - Experience in Cuba

Dr. Rafael Figueredo presented a preliminary report on the status of the National A. aegypti Campaign. During the first half of 1981, the presence of dengue cases caused by virus type 2 was confirmed and cases of DHF were recognized. When this infection achieved the level of an epidemic, a national emergency situation was considered to exist and, on 1 June 1981, the National A. aegypti National Campaign was established to endeavor to permanently eradicate the vector. The Campaign consisted of a preparatory phase 20 days in duration, followed by an intensive phase 2 months in duration, and a consolidation phase 12 months in duration. Finally, the campaign was capped by a surveillance phase which is expected to continue indefinitely.

Initially 6,450 persons were as signed to the various tasks to be carried out and five training seminars were held in 183 places. All the provinces were provided with advice on planning, constructing and equipping a vector control unit (169 in total) in each one of their municipalities. During the intensive phase, activities were focused on the physical destruction of real or potential breeding places; the local population took an active part in these activities, which were supplemented by health education activities in which a wide range of mass media were used. All the premises and houses in the country without exception were treated in weekly cycles including intradomiciliary treatment with non-thermal portable misters for the ultra low volume (ULV) application of malathion at 95 per cent GT as well as extradomiciliary treatment in towns and cities by means of ULV thermal misters using malathion at 95 per cent GT.

In addition, 100 per cent of premises and houses were inspected and focal treatment was applied with the larvacide Temephos (Abate 1.SG) at 1ppm as well as perifocal treatment with a 2.5 per cent Baytex suspension.

During the consolidation phase, all houses and premises were treated in two-monthly treatment cycles with Temephos (focal) and Fenthion (perifocal) in addition to space treatment using Malathion in ultra low volume in towns and cities. Basic sanitation activities were maintained, and a system of surveillance was established, including the imposition of penalties on persons who infringed the sanitary measures

prescribed. The A. aegypti infestation index per house ranged from 0.04 to 20.39 per cent before the beginning of the campaign in 15 provinces of the country. By the end of the third cycle of the consolidation phase, the indexes had fallen to between 0 and 0.19 per cent.

Basic sanitation activities will be stepped up at the beginning of the rainy season in 1982 and intradomiciliary adulticide treatment with malathion will be applied and, for that purpose, the assignment of 5,000 persons to work during that period has been approved.

He noted that the program had been assigned priority by the Governmnt, which had given it its full support and, for that purpose, the understanding of the population had been obtained and its active participation enlisted through a wide and effective health education campaign.

Control in emergency situations

Dr. Robert J. Tonn stated that consideration should be given to strategies for the emergency control of A. aegypti since eradication may not be possible or acceptable for many countries. Emergency control is recommended when an epidemic transmitted by A. aegypti occurs in a neighboring Area. During an epidemic, emergency control may be of limited value in reducing the number of cases, but it can be effective as a pre-epidemic measure.

All emergency plans are aimed at bringing about a rapid reduction in the adult mosquito population and maintaining that low level until the virus disappears from the human population. Ultra low volume applications are the most rapid procedure when infestation affects a large area but they are expensive and can have social repercussions. When the area is small, space treatments may also be effective and be applied with trailor equipment. When there is a risk of DHF or urban yellow fever, the insecticide application method of choice should be the use of spatial aerosols since no dengue vaccine is available and there is a period of latency for the production fo antibodies against yellow fever.

There is usually a considerable lag between the time when an epidemic of dengue is suspected and the virus is identified and an outbreak declared to exist. That calls for the rapid mobilization of vector control activities in order to interrupt transmission and the spread of the epidemic. In most cases, it is advisable to enlist some form of community participation in order to reduce the sources of infestation, and to mention the fact that it makes for good public relations and will help reduce future risks. As far as possible, a dengue or yellow fever surveillance committee should be organized (for example, as part of the Disaster Committees). The Committee should draw up a contingency plan for preventing dengue and instituting intensive vector control, which should be periodically updated; identify areas of risk and check the personnel, insecticides, and equipment available as

well as other potential operating requirements. The important role of informing the public by means of the media available should not be overlooked.

He also stated that training activities should not be made a pretext for doing no field work and that it should be recognized that the appropriate authorities must take a flexible approach that would enable them to change control procedures from a routine phase to a emergency phase.

Reinfestation

Dr. Pedro Luis Tauil pointed out that many countries of the Hemisphere had succeeded in eradicating the mosquito from their territories about 30 years earlier. That had been done at a time when major efforts had been made to control the incidence of urban yellow fever. However, most of the countries had been reinfested and at present there were few American countries that were free of A. aegypti.

The reinfestation of a country will depend on the pressure exerted by the introduction of the vector. The stronger that pressure, the greater the possibilities that the surveillance system will fail. The pressure of the introduction of A. aegypti into a country directly depends on the presence of the mosquito in neighboring countries, the density of the insect populations, and the volume of transportation between the infested countries and those free of the mosquito. The surveillance system should be organized on a epidemiological basis. To determine the receptivity of a region to A. aegypti, a study should be made of the environmental factors, both natural and man-made, such as temperature, rainfall patterns, sanitation conditions, quality of man-made water receptacles. It is very important to identify the common mechanisms of the introduction of the mosquito.

Early detection of A. aegypti is achieved through the systematic inspection of vehicles, traps placed at vulnerable sites and places considered to be strategic. Places that are genuine natural traps, include workshops for the repair of automobile tires, cementeries, scap iron dumps, etc.

International ports and airports are very important places for detecting the initial introduction of A. aegypti. Special surveillance should be exercised, both inside such places and outside them within a radius of 500 meters.

The reinfestation of regions of a country calls for increased surveillance in the other regions so as to prevent the spread of the mosquito. To overcome the difficulties entailed by the control of means of transportation within the country, a rational and practical strategy must be used. It would appear that the most important factor is to

reduce the pressure of the introduction of A. aegypti through the conduct of programs for the control of this mosquito in all the infested countries of the American Hemisphere.

Problems that have impeded eradication

Dr. Marco E. Giglioli pointed out that there are both biological problems and man-made problems that interfered with the eradication of A. aegypti and he made a number of suggestions on activities for overcoming them.

The biological problems included certain aspects of the susceptibility of mosquito populations treated with insecticides. He pointed out that an immediate massive and short-term attack usually resulted in eradication, since A. aegypti does not appear in high density populations, and its range of flight is insufficient to allow it to mate in the presence of an intensive attack with insecticides.

He reviewed the problems caused by man from the period prior to the availability of DDT up to the present. Political, administrative, economic, and educational changes had led to an apathetic attitude towards eradication in many countries. He proposed new approaches aimed at achieving a resolute decision by the government. He pointed out that eradication plans should be presented with a cost/benefit analysis; that programs should be organized on a vertical basis and approved at the highest political level; and that it was necessary to obtain international support; use insecticide application techniques that would minimize the loss of susceptibility of A. aegypti, provide personnel with education equivalent to that of a vector control specialist and conduct a subprogram of applied research on the operational aspects of the eradiction campaign. He concluded that the assignment of priorities to eradication or control is a semantic-policy issue since, to achieve eradication, control must first be obtained.

III. THE HUMAN HOST

Moderator: Dr. L. Charles
Rapporteur: Dr. P. Diggory

Aspects Relating to the Human Population - Experience in Mexico

Dr. Oscar Alfaro stated that an epidemic of dengue type 1 had been underway in Mexico since 1978. Several cities in the country had been affected and the disease had shown epidemiological patterns that suggested the almost universal susceptibility of the human population. In Tapachula and Chetumal, in the south of the country, explosive epidemics with exhaustion of susceptibles had occurred. Recent studies had shown that up to 80 per cent of the population of these localities had antibodies against dengue type 1. In Tampico and Poza Rica on the Gulf of Mexico, epidemic outbreaks had occurred and had been followed by

endemia with seasonal variations. In cities further to the north, such as Matamoros and Reynosa, there had been gradual outbreaks of moderate extent, interrupted by climatic changes during which the cases virtually disappeared. In many other cities, intermediate epidemiological patterns were observed. The infection rate showed marked variations from one sector to another of the communities, which indicated the role of the ecological differences produced by man in the various areas of their habitat.

The spread of the infection throughout the country had followed the routes travelled by the population, which also indicated the role of human habits in the spread of dengue. So far, the symptons observed in Mexico were those of the classical dengue syndrome.

Dr. Eduardo Zorrilla presented observations that endeavored to relate the ecological aspect produced by man in the cities and the extent of the transmission of dengue. In addition to the intensity of A. aegypti infestation, which is related to inadequate methods of storing water and disposing of waste, which may serve as breeding places for mosquitos, the intensity of the transmission of dengue appears to be related to the characteristics of the houses that facilitate the entry of flying insects and, in particular, the population density per square kilometer.

Social Aspects of Dengue Epidemiology - Experience in Cuba

The sociological aspects connected with A. aegypti control programs were illustrated by Dr. Héctor Terry, who referred to the experience gained by the National A. aegypti Eradication Campaign in Cuba during the recent epidemic of DHF.

He emphasized the importance of the material and moral support provided by the Government to the program and described the campaign control methods established by the central, provincial, and municipal governments. He pointed out that the aspects connected with the characteristics of the population, its habits, customs and tradition show that, without the participation of the organized community, neither control nor eradication could be achieved in densely populated areas. He underscored the way in which health education activities carried out on the onset of the epidemic and during the eradication had focused on the inspection of houses, schools, and places of employment for finding actual and potentical mosquito breeding places. He also described the incentives given to residents who had participated in environmental sanitation activities, and the competitive program established by the campaign workers.

Operational Aspects

Dr. Héctor Godoy pointed out that the decisive factor in the success of A. aegypti eradication campaigns is the human factor and reviewed the operational aspects of the campaigns, namely administration, supervision, and operation.

He pointed out that the feasibility of the execution of an eradication campaign implied the existence or creation of a political and administrative organization that would guarantee execution of the activities, and a health organization with broad coverage in rural areas. There should also be an appropriate and prompt response on the part of the Government to the demands of the campaign in the matter of financial and human resources. In addition, there should be legislation supporting all campaign activities, and sufficient administrative flexibility to present interference due to regulations issued by other government agencies.

IV. THE VIRUS

Moderator: Dr. P. Brès
Rapporteur: Dr. D. Gubler

Molecular virology

Dr. Thomas Monath described the use of two new methods in molecular virology: the monoclonal antibody technique and RNA oligonucleotides. Earlier, ascitic fluid from hyperimmune mice (HIMAF) had been used to obtain anti-sera with high titers for seriological tests. Its disadvantage was very heterogenous antibodies and therefore inaccurate tests. A large number of cross reactions occurred, since the antibody against a wide range of antigens was produced. This does not happen with monclonal antibodies since they are homogeneous and very specific. Consequently, they can be used to virus identification.

Dr. Monath reviewed the procedures and methods for producing monoclonal antibodies using the hybridoma technique. At the United States Army Walter Reed Research Institute, four very specific lines for dengue fever had been developed and at present are being produced by the Division of Vector-Transmitted Virus Diseases (CDC) in Fort Collins, Colorado; they are available for distribution to laboratories in many parts of the world. In the past nine months, monoclonal antibodies had been distributed to laboratories in 22 countries.

He also referred to the ARN olingonucleotide trace method for evaluating part of the genoma of the virus. It had been found that there were marked differences between the various serotypes and even between different strains of the same serotype of dengue virus. Therefore, the technique may be used to determine the origin of the epidemic viruses by comparing them with reference strains. So far, dengue-1, dengue-2 and dengue-3 viruses had been studied. Data on dengue-2 virus was presented for illustrative purposes. The virus was classified into six groups on the basis of geographical origin, although some viruses did not fit into the groups.

Finally, he proposed that a study be undertaken for the purpose of systematically analyzing the dengue viruses of the four serotypes known throughout the world, which may be isolated from different epidemics and represent various degrees of seriousness of the disease. Any virus from a new epidemic could be compared with the reference strains. This would provide valid data on the mode of spread of dengue viruses as well as on the changes that may occur in the genoma of those viruses.

Immunization

Dr. Philip Russell said that dengue vaccines should be used for the control of DHF since A. aegypti control had not been effective. He referred to the 17D yellow fever vaccine from the point of view of its efficacy and epidemology and emphasized the differences between the yellow fever vaccine and any future dengue vaccine. He concluded that dengue vaccines would be more efficacious if they were used in an urban environment and that their joint use with vector control measures would have a synergistic effect. He underscored the fact that an effective vaccine against dengue should be safe, low-cost, quadrivalent, produce minimal reactions, be at least 85 per cent effective and induce lasting immunity. Dr. Russell was of the opinion that the production of such a dengue vaccine was possible.

At present, vaccines against the four dengue serotypes are in various stages of production. The degue-2 vaccine (PR 159/SI) had been used in sex tests in humans. The dengue-4 vaccine was at present being tested for the first time in humans. The dengue-1 vaccine was in the production stage and should be available for human tests by late 1982. The dengue-3 vaccine had not yet been prepared, but virus strains for it were being selected.

He described the advances and studies that had been made on dengue-2 vaccine. One of the main characteristics of this vaccine is that in the variety of small plagues, sensitive to temperature, with diminished, neurovirulence in unweaned mice and primates, and producing low viremia. However, it reverts to the virulent form in vitro. Its virulence, genetics, mosquito infection, transmission and production had been widely studied in the laboratory. It is interesting to note that, although it can infect the mosquito both by the parenteral and the oral route, it does not infect the salivary glands and consequently cannot be transmitted. So far, this vaccine had been studied in 147 human volunteers; it had been demonstrated that the production of neutralizing antibodies was better in volunteers that have previously been immunized against yellow fever. This group showed the highest response index as well as a higher immune response to the dengue-2 vaccine. However, reactions in the vaccinees were frequent and included fever, shivers, headache, mialgias, photophobia, eruptions and leukopenia, which are common signs and symptoms.

Dr. Russell ended by stating that another five to eight years were necessary for the development of effective dengue vaccines.

V. THE DISEASE

Moderator: Dr. H. Terry
Rapporteur: Dr. T. Monath

Criteria for Identification and Clinical Management

With respect to the diagnosis of yellow fever, Dr. Peter Diggory pointed out that it was important to inform the medical community that, in addition to occurring in the serious form that gave it its name, this disease can produce very mild manifestations and therefore any suspicion of the disease should be based on epidemiological data. Diagnosis is confirmed by means of seriological tests, virus isolation, and histopathological examinations, in particular of the liver tissue in postmortem studies of fatal cases.

Dengue virus infection may be manifested by the classical syndrome, as DHF, or as dengue shock syndrome. A WHO guide was available for the diagnosis, treatment and control of these syndromes, and was based on practical experience gained in South East Asia and the Western Pacific. The diagnosis of dengue is confirmed by serological tests and virus isolation.

The Role of Laboratories

Dr. Duane Gubler dealt with the epidemiological surveillance of dengue and the role of laboratories in that activity. He pointed out that dengue virus was normally introduced into an area weeks or months before epidemic transmission occurred. This period allowed sufficient time for the adoption of mosquito control measures and identification of the introduction of the virus. Laboratories are of basic importance in the identification process.

Four types of epidemiological surveillance programs were used. First, notification of cases without laboratory confirmation, which makes it possible to detect increases in the frequency of syndromes that suggest dengue, which should stimulate laboratory activities. Second, clinical/biological surveillance should be maintained for the purpose of identifying the dengue serotypes circulating in the community and determining the types of clinical disease associated with dengue infection. This activity calls for the cooperation of the personnel of clincal and laboratory services, although the major responsibility lies with laboratory services. Third, for the early identification of the introduction of more virulent strains, surveillance of fatal virus infections should be undertaken and efforts should be made to isolate the virus from tissue obtained from autopsies on such cases. Finally, it was essential to conduct entomological surveillance to obtain predictive data.

The laboratory procedures available include serological tests such as the hemaglutination inhibition (HI) test, which is easy to perform, requires little equipment, and is reliable although not specific. This test is useful when it is interpreted together with clinical and epidemiological data. The complement fixation test is much more specific and is useful for identifying arboviruses and the antibodies against such viruses.

The plaque reduction neutralization test is useful for typing viruses: it entails some technical difficulty since it requires tissue culture and is not very sensitive to wild viruses.

For virus isolation identification, the methods of choice are the use of mosquito cell lines in tissue culture combined with monoclonal antibodies, which provide rapid results. In the second place, the intrathoracic innoculation of mosquitos, combined with the use of immunoflourescence and complement fixation techniques, is simple and requires little equipment.

Dr. Gubler stated that it was necessary to establish a plan for increasing the number of area laboratories and for updating existing laboratories through a program of short and long-term training in the serological and biological systems that support epidemiology; a mechanism for assuring an adequate flow of reagents and equipment; and a network of communications that will ensure quality control by means of a central reference laboratory.

The DHF Epidemic in Cuba

The session on the disease ended with a detailed report on the characteristics of dengue in the recent epidemic that occurred in Cuba. In 1977, a dengue-1 epidemic occurred and, with effect from May 1981, reports began to be received of cases of dengue with hemorrhagic manifestations in several provinces of the country. By October 10 of that year, 344,203 cases had been reported, of which 10,312 were classified as serious and very serious, and 158 deaths were reported. The initial laboratory studies established that, at the beginning of the epidemic, there was a high proportion of secondary serological responses in patients from which a single specimen was obtained. Subsequently, when paired sera were obtained, high antibody titers against dengue virus were confirmed. The dengue-2 serotype was isolated by means of the innoculation of mice and LLCMK2 cell cultures; immunofluorescence, and plaque reduction were use for the purpose of identification. Most of the patients with DHF showed serological responses that suggested secondary infections, but there were also clinically similar cases with dengue-2 primary infections.

He described the organization during the epidemic for the medical care of adults and of children, respectively. Clear-cut criteria were established for the diagnosis and classification of patients based on the

WHO guidelines, and criteria for deciding on the need for hospitalization and treatment measures were standardized. Early hospitalization and early rehydration were favored. Interferon (30,000-50,000 U/Kg.) was administered to a group of children, and a data suggesting improvement in the course of the disease due to reduction of complications were obtained.

To apply the therapeutic measures selected, boarding schools in the provinces of the country were used as hospitals, a transportation network for the transfer of patients was established, the medical personnel were redistributed, and close supervision of activities was maintained, and the necessary organizational and operational adjustments were made in the light of the course of the epidemic and the avilability of beds and other resources. A total of 116,143 patients were hospitalized and the mortality rate was reduced much below that recorded during similar epidemics in South East Asia and the Western Pacific.

VI. COMPREHENSIVE APPROACH FOR OBTAINING BETTER CONTROL OF THE PROBLEM

Moderator: Dr. Luis Cabrera

Need for Better Knowledge and Understanding of the Epidemiology and Ecology of DHF and Yellow Fever

Dr. Hernando Groot stated that priority should be given to increasing knowledge more directly related to the epidemiology of yellow fever and dengue. There was a need for research on the conditions that determined the urbanization of the jungle virus of yellow fever, including the extent of the contact between man and the vector, the vectoral capacity of the local A. aegypti, the variation in the pathogeneticity of the virus, and its adaptation to Aedes, as well as the interference of antibodies against flavivirus in man.

It was also necessary to gain a better knowledge of the conditions that permitted the persistence of the virus in regions with few monkeys or permitted the frequent reinfection of monkeys. It was necessary to ascertain whether there were other wildlife vertebrate hosts, transoveric transmission, and other vectors.

Research should elucidate the conditions that permit the development of yellow fever epidemics in a typical rural areas, those that favored the meta-enzootic excursions of the virus, and the virological conditions of pathogenesis, and ecological conditions that favored the outbreak of DHF epidemics.

It is necessary to investigate the evolution of endemic dengue, the conditions that favor the movement of dengue virus from one community to another, the biology of A. aegypti and the influence of man on that biology.

Mehtods should be developed for interpreting epidemiological phenomena; they should be capable of being applied rapidly in the field in order to differentiate the immunity produced by yellow fever and that induced by the vaccine, simplify histopathological diagnosis, and identify the various virus strains with simple markers.

The foregoing called for studies that should be made primarily by Latin American research workers and therefore the resolute support of the governments of the Region where necessary. PAHO should strengthen its policy of supporting and promoting the training of research workers and of fostering scientific exchange between institutions interested in yellow fever and dengue.

Improvement of Vector Control Strategies and Program Administration

Dr. Norman G. Gratz referred to the biological factors that should be taken into account when considering the measures that can be adopted to improve the programs.

In the Americas, A. aegypti proliferates almost exclusively in habitats created by man and the density of the mosquito is sufficient in some countries to produce serious epidemics.

There is evidence that the species is now present in geographical and ecological zones from which it was formally absent.

With the exception of the most southern areas and of Canada, Panama, Ecuador, Peru and some Caribbean islands, most of the countries are infested or reinfested since it is known that the vector is usually resistant to cholorinated hydrocarbons and resistence to malathion and Temephos, among other organophosphorus compounds, is already common in the Caribbean.

The risk that outbreaks of urban yellow fever may occur continues to be present, since repeated outbreaks of yellow fever have occurred near cities infested with A. aegypti.

The following administrative factors should be taken into account in evaluating possible improvements in programs:

- The established policy (Resolution XXII of the XX Pan American Sanitary Conference) continued to be the eradication of A. aegypti.
- PAHO endeavors to cooperate with the countries that have programs for eradicating the species or preventing reinfestation.
- In some of the countries in which the infestation is serious and is spreading, the necessary funds and political determination for moving on to eradication are not available despite the regional commitments made.

- The quality of control/eradication programs, where they exist, varies.

- It has been demonstrated that, when there are efficient surveillance and control programs, it is easy to detect and eliminate the reinfestations or infestations that occur.

The measures recommended for improving the present situation are those that can be applied without excessive expenditure at the national level and without radical changes in the policy of the country concerned. These measures include the improvement of training programs, with a view to training more specialists in clinical entomology and increasing the number of universities that can train them. The financing of control programs can be optimized by selecting the most appropriate insecticides, equipment, and surveillance methods; for example, the general use of oviposition traps and calculation of densities of resting adults. It is essential to improve the mechanisms for reducing mosquito breeding places. The installation of piped water supply, health education of the community and, if necessary, legal measures, are areas that can be improved. The prompt recognition of dengue or yellow fever and a more accurate record of the intensity of A. aegypti infestation can facilitate more exact and selective control with less waste and greater efficiency.

Improvement in personnel training

Dr. Luis Jorge Uribe stated that it was necessary to recognize that there was a lack of technical personnel trained in vector control campaigns and that this lack should be made good by appropriate educational programs. It is important to analyze the type of professional or technical personnel vector control programs require as well as the contents of training programs. It appears advisable for professional personnel to be epidemiologists with a wide knowledge of malaria, dengue, DHF, yellow fever, encephalitis, and other vector-borne diseases; they should have a thorough knowledge of diagnosis, pesticide toxology, and the use of new insecticide application techniques, environmental sanitation, reduction of sources, operation and maintenance of equipment, use of new insecticides, and general notions of education, psychology, sociology, anthropology and administration.

Mortality prevention

In the opinion of Dr. Francisco Pinheiro, the role of PAHO in the event of the occurrence of an epidemic could be that of strengthening the surveillance system in the susceptible countries through measures that include the strengthening of the networks of national laboratories for the diagnosis of dengue and the dissemination of information about clinical diagnosis and treatment of the disease. In addition, consultants could be identified and lists of drugs that could be useful in the event of an outbreak could be drawn up. Should an outbreak occur,

PAHO should have available a team of experts in the clinical management and treatment of patients and provide assistance in the form of drugs and other necessary resources.

Future control methods

Dr. Paul Brès stated that 17D yellow fever vaccine had generally proved to be safe and efficacious. It was still being prepared more or less in accordance with the procedures established in the 1940s, but recent tissue culture techniques could perhaps solve the outstanding problems of availability and price.

According to local conditions, preference could be given to one or both of the two following vaccination strategies: attack in case of outbreaks or systematic preventive immunization.

Under a WHO project, efforts are being made in the United States of America and in Thailand to prepare a quadrivalent attentuated virus vaccine against dengue. There were still technical problems to be solved and perhaps another five years would be necessary before the vaccine was on sale. Close attention would have to be given to the trial phases in human subjects in endemic areas where a vaccine of this type could prevent outbreaks with tragic consequences.

VII. CONCLUSIONS AND RECOMMENDATIONS

Moderator: Dr. P. Russell
Rapporteur: Dr. M. Nelson
Dr. H. Groot

A. The Vector

In view of the appearance of an epidemic of hemorrhagic dengue and shock syndrome in the Caribbean and the occurrence of outbreaks of jungle yellow fever near cities with a high density of A. aegypti in the Americas, the Group concluded that the eradication of A. aegypti is technically feasible in the countries of the Region. However, there were a number of important constraints that may at present frustrate the success of the program at the regional level.

Recommendations

1. Each country should make vigorous effort to eradicate A. aegypti or reduce its density to the lowest possible level, in accordance with its technical and financial resources and its national priorities. In any case, the density should be reduced and kept at a level at which it is difficult for disease transmission to occur. This should be supported by efficient programs of surveillance both of the vector and of the disease.

2. Taking into account recent experience of the economic and social impact of dengue and yellow fever epidemics, each country should think about the cost/benefit of vector control compared with the effect on health, since the value of the loss of lives is incalculable. Each country should draw up a national plan tailored to its own circumstances, which includes the following points:

a) Diagnosis of the present situation, based on the problem of the presence of the vector in its territory and the risk of the transmission of dengue and yellow fever to its inhabitants and those of neighboring countries.

b) Surveillance of the vector and of the disease through the use of appropriate resources in the areas of morbidity and serological, biological and entomological evaluation.

c) Operational and epidemiological research.

d) Evaluation and strengthening of the effectiveness and efficiency of its control methods, including the protection of ports, airports and border areas.

e) Training and motivation of personnel at all care levels of the health sector to induce their participation and cooperation in vector control activities.

f) To enlist the participation of other sectors (such as those of water supply, excreta and waste disposal, education, and the private sector) in the eradication of the vector.

g) To enduce in the population a health awareness of vector control through the sanitation of housing.

3. The known integrated methods for the control of pests have been adequate to achieving the goal of eliminating the vector in a number of countries, where they have been applied sufficiently vigorously and with the necessary coverage. However, some ecological, biological and financial factors are impeding and now threaten the application of those methods at the regional level. Nevertheless, research on new methods should be vigorously pursued. Pending the results of that research, the present A. aegypti campaigns should put greater emphasis on the application of legislative measures as well as on the education of the community, integration of control methods, rigorous supervision and discipline in field operations, and the selective treatment of highest-risk areas when the simultaneous coverage of the entire country is not possible.

4. Because of recent infestation of countries that had succeeded in achieving eradication, the Group emphasized the importance of maintaining strict surveillance in the vector-free countries so as to promptly detect any reinfestation and eliminate it before it spreads.

5. Since the general purpose of eradication will not be achieved in the short term by all the countries of the Region and in view of the risk of the occurrence of new dengue epidemics and the threat of the urbanization of yellow fever, the Group recommends that each government draw up an emergency plan that includes an inventory of the resources available in the country and in the neighboring countries as well as an operating program that can be put into place should an epidemic occur.

6. Recognizing that knowledge about the vector and its control are incomplete and bearing in mind the recent findings concerning its habitat and distribution, the group recommends that research be conducted in the following areas:

a) Biology, ecology and distribution of A. aegypti in both its larval and adult stages, in different breeding places, in order to develop new survey methods which are more efficient and provide indexes of the transmission of the disease and the genetic variations between the different geographic strains in their vectoral competence, their behavior, and their susceptibility to insecticides.

b) The effectiveness of new insecticides and safe and low-cost methods of application.

c) Alternative methods such as those for biological control by means of pathogens, parasites, and predators of A. aegypti and biological products.

In fulfillment of these recommendations, PAHO/WHO should undertake:

1. To coordinate the effort to aid the individual countries to adapt the general guidelines to local conditions.

2. To foster the exchange of operational and research experience between neighboring countries and regions that have a common interest in vector control.

3. To strengthen the self-sufficiency of the countries to enable them to train their own vector control personnel.

4. To continue efforts to focus the attention of the Member Countries on the priority that should be assigned to the national A. aegypti campaigns.

5. To take all necessary steps to enable each Member Country to promptly obtain the necessary equipment and materials for use during epidemic outbreaks of diseases transmitted by A. aegypti and in A. aegypti eradication and control programs considered priorities by the national authorities.

6. In cooperation with the Member Countries, to endeavor to make a realistic evaluation of the cost of an eradication program of limited duration for the Hemisphere and of the cost of the present control programs both for the Member Countries and for PAHO.

B. Epidemiological Surveillance

The experience gained with epidemic outbreaks of dengue and more recently of DHF in the Region, in the presence of high A. aegypti densities and in view of the generally unsatisfactory results of programs for the control of this vector, it is essential that the scope and quality of the epidemiological surveillance of the syndromes of this disease be assigned the highest priority if the health authorities wish to alert serious disasters in this area in the future.

In addition, the new generations of physicians have little knowledge of yellow fever and almost never take it into consideration in their differential diagnoses. Nor has there been any improvement in the quality of the diagnosis of febrile diseases, which is almost exclusively based on clinical appraisals without making use of the available laboratory resources. Since this is happening at a time when many cities, because they have been reinfested with A. aegypti, offer fertile ground for the outbreak of epidemics of jungle yellow fever, with all the drama and tragedy that entails, an urgent appeal is made to the countries of the Region to strengthen their surveillance activities.

Recommendations

1. Each national health organization should establish and continually strengthen a system for obtaining, tabulating, and analyzing epidemiological data that include information that suggests or confirms the occurrence of dengue, DHF and yellow fever. The purpose of this system should be as follows:

a) Identification of population groups with a high risk of exposure to dengue as well as of the factors associated with its occurrence and distribution.

b) Identification of geographical areas exposed to a high risk of the occurrence of dengue.

c) Maintenance of a high level of alert to the possibility of the occurrence of classical dengue fever, DHF/shock syndrome, so as to make it easier to promptly detect and notify cases.

d) Availability of national or reference laboratories for confirming cases of dengue, including identification of serotypes.

e) Prompt provision of information to vector control programs to ensure that the necessary measures are applied in high-risk areas and to prevent the spread of dengue.

f) Provision of regular analyses and of information to health personnel on the surveillance of dengue and of DHF at the national and regional levels. This analyses should, if possible, be made locally.

2. Countries infested with A. aegypti should review their dengue and yellow fever surveillance activities for the purpose of evaluating coverage, methodology, and techniques used, quality of laboratories, and training needs.

3. National laboratories in high-risk areas should at least be capable of making routine serological diagnoses, but they should also be encouraged to acquire a virological capability. Wherever possible, the establishment of high levels of competence should include:

a) Production of diagnostic antigens.

b) methods of mosquito or mammal cell culture for the possible isolation of virus demonstrated by immunofluorescence.

c) Identification of the virus by means of immunofluorescence using monoclonal antibodies specific to one type.

d) Cell cultures for plaque reduction neutralization tests.

4. The epidemiological surveillance of DHF must be adapted to the epidemiological situation of each region or country (areas in which DHF/shock syndrome cases exist), primarily for the purpose of preventing the spread of the disease and deaths.

5. Health personnel working in high-risk areas infested with A. aegypti should be familiar with the clinical symptons of DHF. The health services should establish a system designed to maintain awareness of DHF as a potential problem; to maintain an inventory of medical care facilities and human resources, laboratories and hospitals that should be available in the event of an outbreak; and to prepare guidelines for ensuring the priority hospitalization of high-risk patients to ensure their correct treatment.

6. In dealing with patients during a DHF epidemic, the following aspects should be given priority attention:

a) The prompt hospitalization of dengue patients in order to prevent hemoconcentration in those patients that present vomiting and petechias or to treat them to prevent shock.

b) The prompt treatment of shock since, in those patients in which it is prolonged, serious complications may occur, including severe hemorrhages (hematemesis, melenas, hematurias and others), and death ensue.

7. Equipment should be available for measuring the corpuscular volume with the hematocrite in all centers for the diagnoses and treatment of DHF.

8. The surveillance of yellow fever should be stepped up in all enzootic areas and should be based, in accordance with the pertinent manuals, on the early detection of virus activity (either through observation of the study of monkeys or more commonly through the confirmation of human cases based on virus isolation or examination of the liver). In addition, the enzootic area, the population exposed (in order to be vaccinated) should be accurately identified, as should be logging or agricultural activities in forests, the development of land settlements, and migratory flows to the area. Receptive jungle areas should be placed under surveillance so as to detect the possible arrival of the virus there.

9. The quality of the diagnosis of febrile diseases should be improved in localities infested with A. aegypti by studying the livers of persons, who die from those diseases, all of which should be accompanied by vaccination, if indicated and, should the existence of any yellow fever patient be confirmed in the locality, the necessary means for immediately controlling A. aegypti should be available.

10. The laboratories of the country should be strengthened to enable them to identify viruses and study liver specimens. If that is not possible, immediate contact should be established with other institutions so that they can do so instead. The plan for the strengthening of laboratories should be such as to enable them to carry out simple and rapid techniques and procedures for identifying viruses, including the use of monoclonal antibodies.

11. Information on proven and suspected cases of yellow fever should be promptly communicated both to the authorities of the country and to PAHO.

The role of PAHO/WHO in implementing these recommendations should be one of:

1. Promoting the use and assisting in obtaining and analyzing oligonucleotides of all strains of epidemic dengue.

2. Rapidly moving a group of previously identified experts so they can cooperate with the countries and pass on to them their experience in clinical diagnosis, patient management, and treatment. PAHO should draw up a list of all the drugs, materials and equipment necessary for the treatment of severe cases of

dengue and should promptly provide assistance to the countries that encounter difficulties in obtaining them, particularly materials produced abroad.

3. Carrying out a technical review of the classification of DHF published by WHO in 1980 (WHO, Technical guides for diagnosis, treatment and control of dengue haemorrhagic fever. Technical Advisory Committee on dengue hemorrhagic fever for the South East Asia and Western Pacific Regions, 1980), taking into account the experience of Cuba in 1981.

4. Promoting projects for the collection and analysis of representative strains of jungle yellow fever virus from all the enzootic areas.

C. Vaccine

So far the yellow fever vaccination policy has consisted primarily in vaccinating workers, visitors, immigrants and other exposed persons in enzootic areas. This policy needs to be reviewed in the light of the recognized potential risk caused by the extensive reinfestation and spread of A. aegypti.

A program for the modernization of yellow fever vaccine production will be essential if the increased needs for immunization of populations at risk in the enzootic area and areas nearby are to be satisfied. This would be congruent with one of the objectives of the Plan of Action for the implementation of the Regional Strategies for attaining the goal of health role by the year 2000.

Recommendations

1. To enlarge the population that should be immunized on a priority basis to include the residents of communities located in areas in which jungle yellow fever is active, the residents of towns and cities infected with A. aegypti that area near foci of jungle yellow fever, and the residents of urban centers infested with A. aegypti that have frequent contact with the jungle yellow fever area.

2. To maintain group immunity through the regular and systematic vaccination of children and immigrants.

3. To study the possibility of including yellow fever vaccination in the Expanded Program of Immunization (PAI) in the high-risk areas defined above.

4. The recommendations of the Symposium on Yellow Fever sponsored by PAHO in Belem in 1980 are reaffirmed.

5. It is recommended that the cold chain already developed by the PAI be adopted in order to meet the needs for the appropriate storage and transportation of yellow fever 17D vaccine.

6. It is recommended that the countries that produce malaria vaccine encourage the production laboratories to package it in ampoules that contain a number of doses compatible wth the operating conditions for its application.

7. To recommend that the countries that provide malaria vaccination conduct regular serological surveys in the vaccinated population for the purpose of the quality control of that vaccination.

D. Research

Although considerable knowledge is available on the epidemiological background and ecology of yellow fever, many questions are still unsolved. The annual incidence of jungle yellow fever that has been reported has continued to be the same or has increased, and the possibility of urban epidemics is a real one. There is an urgent need for additional and thorough research designed to understand the mechanisms by which the yellow fever virus maintains itself in the enzootic cycle, the reasons for its periodical recrudescence, and the factors involved in its spread, including the interface between the jungle cycle and the areas infested with A. aegypti. This research will call for a multidisciplinary approach in an appropriate area in which the jungle activity of yellow fever is close to A. aegypti infestations.

More information must be obtained about the actual prevalence of jungle yellow fever in man, the transmitting capacity of A. aegypti with various South American strains of yellow fever based on characterization of mosquitos by izoenzymes.

The possible variation of virus strains as regard virulence and capacity to produce viremia in monkeys associated with the jungle cycle such as Alouatta and Ateles. More information must also be obtained about Haemagogus and its capacity to be infected with various South American virus strains and its distribution in non-jungle rural areas, the various possible vectors of Haemagogus in non-jungle rural areas, the dynamics of a non-human primates in enzootic areas, the role of marsupials and snakes e.g. Bradipus, Coendu) in enzootic places with few monkeys and the interference of immunity to dengue by yellow fever infection using Alouatta and other American monkeys as experimental animals.

Furthermore, epidemiological research on the factors that influence the transmission of epidemic dengue is essential to the prevention and control of this disease and priority should be assigned to the following research areas:

a) Studies on the relation between the transmission of the disease and the behavior, ecology, genetics, physiological age, and vectoral capacity of A. aegypti.

b) Development of new methods and indexes for evaluating A. aegypti density that more accurately reflect the relationship between the density of the mosquito and the transmission of the disease.

c) The determination of the relative risk of DHF/shock syndrome in patients with primary and secondary infections, including possible variations due to ethnic and nutritional factors.

d) Studies of the behavior of dengue virus in endemic conditions and "shift" of dengue virus from one place to another.

e) Further studies on anti-virus drugs and on interferon in the treatment of dengue and yellow fever.

Methods for the serology of dengue and the isolation of the virus that include a number of serological tests that use of ELISA method and virus identification by means of immunofluorescence with monoclonal antibodies are being prepared and tested. The preparation and field use of simplified techniques that do not make it necessary to depend on a laboratory specialized in arboviruses or on high-cost equipment, should be supported by PAHO as part of a program to improve laboratory assistance for surveillance at the national or lower levels.

Recommendations

1. That the governments of the Latin American countries that face dengue and yellow fever problems promote research on these diseases, especially that which must necessarily be conducted locally.

2. That PAHO sponsor additional research initiatives on the epidemiology and ecology of dengue and yellow fever that include multidisciplinary approaches, so as to respond to the principal questions posed; support for these initiatives should be obtained through interested national and international agencies.

3. That PAHO sponsor the training of virologists and epidemiologists in Latin America and the Caribbean who are working in the field of dengue and yellow fever.

4. That PAHO sponsor the cooperation of research centers in Latin America and the Caribbean with institutions in other parts of the world that are interested in dengue and yellow fever research.

Annex

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