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Prevention of Rheumatic Fever

Acute rheumatic fever (ARF) and chronic rheumatic cardiopathy (CRC) are high on the list of causes of death from cardiovascular disease among adolescents and young adults. These diseases are also a common cause of morbidity and extended disability.

In recent decades the incidence of acute attacks of rheumatic fever has declined sharply in developed countries and also, but to a lesser extent, in developing ones. This may be associated not only with medical measures but also with better general living conditions in many communities.

CRC. on the other hand, continues to be a significant though diminished cause of morbidity, disability, and mortality, as a secondary consequence of severe, past attacks of rheumatic fever. This holds true for developing countries and also some developed countries.

According to statistics on ARF and CRC mortality in the United States, between 1940 and 1962 the rate per 100,000 inhabitants declined by nearly one-half in the 25-44 year age group and to almost one-eighth in the 5-24 year age group.

Information available on hospital discharges shows that ARF and CRC are still important causes of morbidity. Data from four countries—Canada (1972), Ecuador (1973), Paraguay (1975), and Venezuela (1973)—indicate the following:

In the total population, of every 1,000 hospital discharges of patients admitted for all causes, the proportion of ARF patients ranged from 0.5 in Canada to 1.7 in Paraguay and Venezuela. In the 5-14 year group the proportion was also low in Canada (2.2), but reached as high as 6.1 in Ecuador, 9.4 in Venezuela, and 11.5 in Paraguay. The proportion declined in the 15-24 year group, in which the highest rate was 2.2 in Venezuela. The decline was even greater in the 25-44 year group.

CRC as the cause of hospitalization of patients subsequently discharged ranged from 0.1 in Paraguay to 2.4 in Canada. These figures are based on hospital discharges of patients in all age groups.

Figure 1 provides the latest available information on ARF and CRC death rates in six countries of the Americas: Argentina (1978), Canada (1977), Cuba (1977), Guatemala (1976), Mexico (1974), and Venezuela (1977).

Acute attacks of rheumatic fever occur most frequently between the ages of 5 and 15, after which the frequency declines. They seldom occur in children under 5.

ARF may attack the joints, the heart, and the central nervous system. Its most important clinical manifestations are arthritis, carditis, and chorea. The joints are the most common but least important site of the disease, as there is no permanent damage. CRC is more serious because it poses a direct threat that persists beyond the acute stage, can cause permanent damage, and may evolve unfavorably and become graver if there are further attacks of ARF.

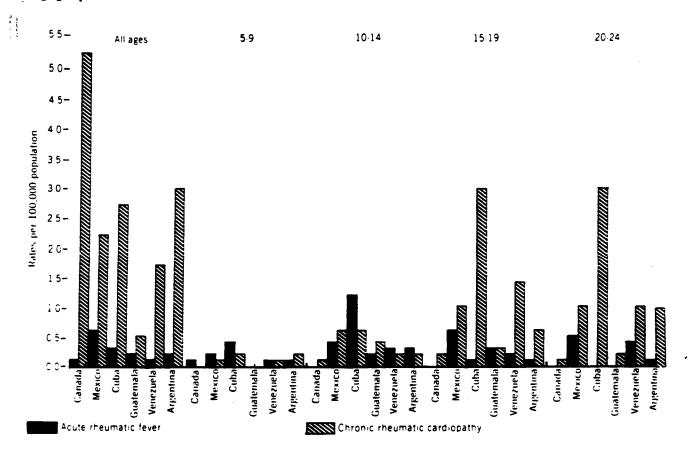
There is a close relationship between ARF and the in-

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Figure 1. Mortality due to acute rheumatic fever and chronic rheumatic cardiopathy in six countries of the Americas, by age-group.



fection caused by group A beta-hemolytic streptococci, of which ARF is a non-suppurative complication. After the onset of streptococcus infection (and following a latent period of 1-3 weeks), clinical manifestations of ARF may appear in susceptible persons. The factors determining this susceptibility are not at present known.

All children in the group at greatest risk (5-15 years) suffer an average of one infection of the respiratory tract per year. If this infection is due to group A beta-hemolytic streptococci, there is a risk that an attack of ARF will follow the infection. Even under nonepidemic conditions, this will occur in 3 or 4 of each 1,000 infections. In special situations, particularly in closed environments (asylums, barracks, etc.) that favor the dissemination of germs, the proportion increases to 3 or 4 per 1001 infections.

There are more than 60 types of group A beta-hemolytic streptococci, with no cross-immunity among them. For this reason, a person who has been infected by a given type is immunized only against that particular type but remains susceptible to all other types of streptococci. The risk of streptococcus infection may therefore be considered a continuing possibility.

People who have had rheumatic fever are at high risk of suffering a new and severe attack if again infected by streptococci. This risk increases directly and proportionately with the following factors: the youth of the patient; the number of earlier attacks of ARF: the severity of the residual cardiac lesion (CRC): the closeness in time between the last acute attack and the new streptococci infection; and the number of days elapsed between the onset of the infection and the beginning of treatment to eliminate the streptococci.

The prevention of streptococcus infection was proposed a long time ago and is now being applied, although regrettably not on as wide a scale as desirable.

Rheumatic cardiopathy is one of the few chronic cardiopathies that can be prevented by means at present available. The ideal way to prevent it would seem to be to prevent the initial attack of rheumatic fever by warding off the streptococcus infection or treating it promptly when it appears (primary prevention). Since there is no way of identifying those susceptible to rheumatic fever, it would be advisable to protect the entire population, or at least those in the age at greatest risk, but this would not be practicable as a control measure.

However, it is possible to focus preventive action on the

¹Stamler. Cardiología preventiva. Barcelona, Editorial Científica Médica, 19⁷0, p. 382.

groups at greatest risk, such as people who are known to be susceptible because they have suffered from rheumatic fever or have had a chronic rheumatic cardiopathy. Such action lies in adequate treatment or prevention of rheumatic infection. Either way, an attack of ARF and, consequently, cardiac damage, are prevented (secondary prevention).

Results throughout the world have shown the beneficial effects of applying these measures. Limited experiments conducted in specialized centers in seven countries of the Region participating in a PAHO-coordinated collaborative study have demonstrated the feasibility of control programs aimed at selected groups in the community. Centers in Argentina, Bolivia, Brazil, Chile, Ecuador, Peru, and Venezuela are participating in the study, in which 2,500 patients with active rheumatic fever or a history of having had the disease were initially registered. The patients are being kept under treatment with monthly injections of benzathine penicillin, and their adherence to the treatment and the clinical evolution of the disease are checked yearly.

Preliminary results indicate that when patients are examined periodically and receive their preventive injections on a regular basis, protection against further streptococcus infection is effective in direct proportion to the regularity of the treatment. In 1,110 patients that were receiving monthly intramuscular injections of benzathine penicillin, the number of streptococcus infection detected during the year of observation was recorded and correlated with the number of monthly injections received. It was found that the percentage of patients remaining free of streptococcus infection increased in direct proportion with the strictness of observance of the preventive regime, as shown in Table 1.

The most commonly used schemes of preventive treatment are indicated below:

For primary prevention, the following scheme is recommended for early treatment of streptococcus infection:

Benzathine penicillin, intramuscular injection, 1 injection

Dose: 1,200,000 units for patients 6 years or older 600,000 units for children under 6

Erythromycin. oral. every day for 10 days*

Dose: 250 mg. 4 times per day, for patients 6 years or older

125 mg. 4 times per day, for children under 6

For secondary prevention of rheumatic fever, those susceptible will be protected by the following scheme:

Benzathine penicillin, intramuscular injection, once per month, for a number of years

Dose: The same as indicated for the treatment of the infection

OF

Sulfadiazine, oral, every day, for a number of years

Dose: 1 g per day for patients 12 years or older

0.5 g for patients under 12

If streptococcus infection occurs during the interval between penicillin injections in a patient who has been following this preventive scheme, or if the patient takes sulfadiazine at any time, the patient should be given an intramuscular injection of benzathine penicillin at the proper dose for age. It is imperative to note that sulfadiazine is generally effective as a preventive agent but should never be used to treat an infection that already exists.

The prophylactic schemes should be widely publicized so that they become a part of the habitual therapeutic methods of general physicians and are known and applied at all levels of medical care services, including the primary level.

In developed countries with the necessary resources for providing adequate medical care, primary prevention is carried out by specifically treating the streptococcus infection after it has been identified by bacteriologic examination (culture of the pharyngeal exudate). This system requires a waiting period of 18-24 hours to determine the test results. This delay does not imply an important risk because the treatment to eliminate the strep-

Table 1. Cases of rheumatic fever with results of first yearly examination, classified according to number of attacks of streptococcus pharyngitis from the time of initial registration and to regularity of preventive treatment.

No. of injections of benzathine penicillin in 1 year	Streptococcus pharyngitis								
	Total None		One		Two or more		Suspected		
	(100 مى)	No.	o 7.0	No.	0.0	No.	σ,	No.	σ,
11-12	989	928	93.8	25	2.6	9	0.9	2-	2.1
8-10	70	58	82.6	6	8.6	2	2.9	4	5.1
0-7	51	40	78.4	1	2.0	-	-	10	19.6
Total	1.110	1.026	92.4	32	2.9	11	1.0	41	3.

^{*}It is very important to remember that when the treatment is given orally this dose should be maintained for the entire period of 10 days, even if the clinical state of the patient improves.

tococci. if correctly applied, is effective if given at any time during the first week of this infection. Once the infection is confirmed, the patient is treated with the appropriate antibiotic. The rules of sound medical care should be applied, with no unnecessary administration of antibiotics.

In order to apply successfully the preventive measures at community level, it is necessary to employ strategies that make it possible to obtain optimum results with simple, effective, and acceptable elements. If treatment of the streptococcus infection is to be delayed until the infection is confirmed by bacteriologic examination (culture of the pharyngeal exudates), the patient should visit the medical care facility twice after the findings are known.

These requirements are applicable and beneficial when circumstances allow them to be applied, but this is not always feasible in the context of a control program, the end of which must be to protect large population groups. Efforts to apply the scheme could lead to difficulties that would prevent the program from achieving wide coverage, since in many parts of the Region there are population groups that have little access to fairly sophisticated medical care facilities. For proper coverage the protective measures should be applied at all levels, including, if possible, the primary level. In order to attain this latter objective it is advisable to include, as routine tasks, some of the procedures related to the control measures mentioned above. These procedures would include, among others, the identification of cases of infection of the upper respiratory tract which is very likely to be caused by streptococci, treatment with an injection of benzathine penicillin in accordance with the proposed scheme, and, when appropriate, the application of secondary prophylaxis to patients who have suffered from rheumatic fever.

The activities to be carried out at various levels of the health care services should be programmed so as to allow optimal utilization of available resources. A guide for the programming of activities, including the allocation of functions to staff and calculation of necessary resources, as well as a guide for supervision and evaluation, form part of the publication prepared by PAHO entitled Normas de prevención de la fiebre reumática en la comunidad, which will be published in 1980.

It is anticipated that the guides proposed by PAHO can be adapted to the local requirements and resources of the countries that consider it necessary to do so.

It may be possible to solve the health problem of ARF and CRC when an effective vaccine is available for the various types of streptococci, and such a possibility is being investigated. At this time, however, the solution best geared to the means now at hand lies in wide and continuous application of the preventive measures described above.

(Source: Noncommunicable Disease Unit, Rheumatic Fever Prevention Program, PAHO.)

Notification of Communicable Diseases in the Americas

The international notification of communicable diseases in the Americas is mandated by Articles 3-8 of the Pan American Sanitary Code and Part II of the International Health Regulations. The Pan American Health Organization receives information from the following sources:

- Telegrams from the countries of the Region reporting cases of diseases subject to the International Health Regulations or of alarming situations, outbreaks, or epidemics of other infectious diseases.
- Weekly and/or monthly statistical reports prepared by the ministries of health of the countries and supplied on the PAHO international form.

• Epidemiological bulletins (see Table 1) and other official publications of the ministries of health.

PAHO, in turn, relays the epidemiological information of international interest to the countries pursuant to the Pan American Sanitary Code and the International Health Regulations. It does so in the following way:

- 1. When a Member Country notifies PAHO of cases and/or deaths due to diseases covered by the International Regulations, this information is immediately relayed to all the countries of the Region by telegram.
- 2. The data mentioned in paragraph 1 are also relayed by telegraph to WHO Headquarters in Geneva, where

Diseases Subject to the International Health Regulations

Cholera, yellow fever and plague cases and deaths reported in the Region of the Americas up to 30 June 1980

Country and administrative subdivision		Yello	Dia	
	Cholera Cases	Cases	Deaths	Plague Cases
BOLIVIA	_	22	18	_
Cochabamba	_	11	10	_
La Paz	-	11	8	-
Brazil*	_	11	9	27
Ceará		_	-	27
Goiás	_	9	9	_
Maranhão	-	2	_	. —
COLOMBIA	_	2	2	_
Cesar	_	1	1	_
Norte de Santander	-	1	1	-
PERL'		21	18	_
Ayacucho	_	8	-	_
Junin	-	5	3	_
San Martin	_	7	-	
•••	_	1	1	_
United States .	8	_	_	_
California	6	-	_	_
Pennsylvania	1	_	_	_
	1	_	_	_

^{*}One case of yellow fever in Pará was eliminated because it had not been confirmed.

they are included in the Automatic Telex Reply Service (ATRS). This service operates around the clock, and the information is available to the countries, which can obtain it by calling telex No. 28150. When the call is made, there is an exchange of identification codes and the code letters ZCZC are given, followed by ENGL to obtain the reply in English or FRAN to obtain it in French. The message is then automatically transmitted to the requestor. It is important that this procedure be followed exactly and that the operator wait, without doing anything else, after giving the symbols for the desired language, as otherwise the automatic response is interrupted. The end of the message is indicated by the letters NNNN, after which the operator making the call should again exchange identification codes and terminate the communication.

The cost of leasing and operating the telex machine is

borne by WHO; the cost of the call, which is modest, is paid by the caller.

If additional information is needed, this may be requested of WHO Headquarters (Communicable Disease Epidemiological Surveillance), by telephone (Geneva 34 60 61, extension 2624), by telegram (EPIDNATIONS GENEVA), or by telex, number 27821. It is important not to confuse this telex number with the ATRS number since use of the latter number for normal transmission of messages can lead to delays or annul the messages.

- 3. Daily transmission to the countries of the Region of the information provided by WHO through ATRS on the occurrence, in any country of the world, of cases and/or deaths due to communicable diseases of international importance.
 - 4. The PAHO Epidemiological Bulletin, which pro-

⁻None.

^{...} Data not available.

Table 1. Epidemiological bulletins of the countries received at PAHO.

Country	Publication	Frequenc
Argentina	Boletin Epidemiológico Nactonal	Monthly
Bolivia	Buletin Epidemiológico	Monthly
Brazil	Boietim Epidemiológico	Fortnightly
Canada	Canada Diseases Weekly Report	Weekly
Chile	Vigilancia de Entermedades Trans-	•
	misibles v Zoonosis	Monthly
Colombia	Boletin Epidemiológico Nacional	Monthly
Costa Rica	Semana Épidemiológica	Weekly
Cuba	Boletin Epidemiológico	Monthly
Dominican	,	•
Republic	Comentarios Epidemiológicos	Monthly
Ecuador	Buletin Epidemiológico Semanal	Weekly
El Salvador	Reporte Epidemiologico	Monthly
Honduras	Boletin Mensual de Entermedades	•
	Transmisibles	Monthly
Panama	Boletin Epidemiológico	Monthly
Paraguay	Boletin Estudístico-Epidemiológico	Monthly
Puerto Rico	Informe Epidemiológico	Monthly
United States	Morbidity and Mortality Weekly	
	Report	Weekly
	CDC Veterinary Public Health Notes	Weekly
Venezuela	Boletin Epidemiologico Semanal	Weekly

vides a summary every two months of the epidemiological situation of the diseases subject to the International Health Regulations in countries of the Region, as well as other epidemiological studies of regional interest. Other periodic publications such as the Boletin Informativo of the Expanded Program on Immunization and the Boletin of the Pan American Zoonoses Center contain reports on other diseases of interest to the Region; the Boletin Epidemiológico of the U.S.-Mexico Border Public Health Association and the Surveillance Report of CAREC are concerned primarily with epidemiologic situations of subregional interest.

5. Other publications, such as PAHO's Annual Report of the Director, which supplies general information on disease control programs in the Region, Health Conditions in the Americas, and Reported Cases of Notifiable Diseases in the Americas, include statistical data supplied by the countries on communicable diseases.

Malaria Program in the Amazon Region of Brazil

Amazonia accounts for 73 per cent of the malarious area of Brazil, as indicated in Figure 1, but its population is only 20 per cent of the total population of that area. Eradicating malaria from the Amazon region is considered a long-term undertaking, owing to factors that make it difficult to control the disease or that even favor its transmission.

The obstacles to malaria control include low demographic density, dispersion of the population, existence of nomadic groups, difficult access to areas close to the tributaries and subtributaries of major rivers during the dry period in the second half of the year, and flooding of fields in the second half of the year. The continuous migratory flows from areas free of transmission to Amazonia are assuming considerable importance in the epidemiology of malaria and are responsible for the heightening of the endemia in various parts of the region.

The factors that favor malaria transmission are associated with environmental conditions propitious to the maintenance of the endemia, such as temperature, humidity, and rainfall, which influence the life and development of the vectors.

Special mention should be made of the ramshackle construction of houses in the region, which allows the entry of man-biting mosquitoes, thereby contributing to transmission and, consequently, maintenance of the endemia.

Technical Problems

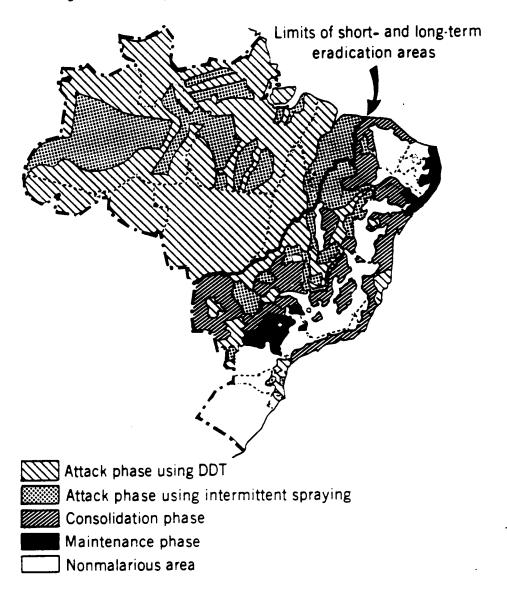
In Amazonia there are technical problems associated with parasites, vectors, and human groups.

In regard to parasites, studies initiated in 1961 in five states and territories (Amapá, Amazonas, Pará, Rondônia, Roraima) proved the existence of chloroquine-resistant strains of *Plasmodium falciparum*.

Insofar as vectors are concerned, Anopheles darlingi is the most important species: though susceptible to DDT, in some places where wall-less or uncompleted houses predominate it is able to transmit malaria because there are no potential landing places that can be sprayed.

With respect to man, his habits, and environment, there are problems that exert a sharp influence on the epidemiology of malaria. In keeping with Brazil's overall development policy and the aim of increasing the density

Figure 1. Areas and phases of the malaria eradication program, Brazil, 1978.



of population in hitherto uninhabited areas, the Government is promoting and conducting agricultural, settlement, mining, and hydroelectric projects, as well as highway construction. These projects have attracted migratory flows of workers and their families from other regions. Some of the migrants return to their places of origin, thereby spreading malaria to the areas or regions where it was no longer being transmitted.

Despite the fact that the Superintendency of Public Health Campaigns (SUCAM) performs semiannual house sprayings as a regular activity under development projects and collects blood samples and provides treatment to individuals with fever, the incidence of malaria has not diminished significantly. The concentration of SUCAM's work in areas at greatest risk increases the

number of positive tests, sharply distorting the parasite indexes because of the many houses inspected more than once with positive results.

Tables 1 and 2 show, respectively, the number of DDT house sprayings $(25/m^2)$ and the parasite rates in 1978.

Studies Toward the Solution of Problems

Considering the technical problems that have hampered malaria eradication in Amazonia, as well as the possibility that the problems may become more serious, studies in the fields listed below are urgently needed:

• Malaria chemotherapy. Study of the susceptibility of *P. falciparum* to antimalaria drugs: study of the efficacy

of the new schemes for treating P. vivax infections; and, finally, clinical tests and field studies of new drugs.

- Immunology. Serologic tests for use in diagnosis and epidemiological surveillance.
 - Study of the ecology and biology of vectors.
- Control methods. Application of new insecticides in various epidemiologic situations, biological control of vectors, and combined methods.

Aware of these needs, SUCAM, with advisory assistance from PAHO/WHO, is undertaking the following research: study of the problem areas of Amazonia, in order to determine the reason for difficulties in applying control measures and to propose new methods in this field; tests of a new antimalaria drug (mephloquine) for use against chloroquine-resistant strains of *P. falciparum*, which are slated to begin during 1979-1981 in Pará State.

The Amazonia Development Superintendency

Table 1. Data on spraying, 1978. (Long-term area)

Regional divisions	Directly protected population	No. of houses sprayed
Acre	210.928	47,727
Rondônia	287.077	74,324
Amazonas	313.949	80.609
Roraima	49.905	13.051
Amapá	119.514	24.056
Para .	1.521.179	384.306
Maranhão	1.969.941	560.537
Goiás	559,042	163.317
Mato Grosso	588.422	154.767
Total	5.619.957	1.502.694

Source: SUCAM.

Table 2. Number of slides examined, number positive, and parasite indices, 1978.

D !1	No. of	slides	Index of	Annual parasite index	
Regional divisions	Examined	Positive	positive slides		
Long-term eradication		•			
Acre	32,779	6,331	19.3	23.2	
Rondônia	96.045	27,989	29.1	175.0	
Amazonas	81.699	4,698	5.1	4.0	
Roraima	29.971	7,233	24.1	136.0	
Amapá	21.494	6,829	31.7	42.4	
Pará	289,140	30,150	10.4	10.7	
Maranhão	313,967	13,593	4.3	3.8	
Goiás	34.796	1,993	5.7	2.3	
Mato Grosso	61.711	6,815	11.0	8.7	
Total	961.602	105,631	10.9	10.7	

Source: SUCAM.

(SUDAM), which is responsible for coordinating regional development, undertook a study, together with the ministries of health, social welfare, education and culture, and labor to define the minimum conditions for providing health and education services to workers of companies operating in the Amazon region.

Article 2 of Resolution 3.750 79 of the Governing Board of SUDAM provides as follows:

The minimum health and sanitation service to be provided to personnel of the company shall have the following objectives:

- Protect the population against regional endemias and prevent the introduction of endemic diseases not present in the Region, through measures with collective coverage.
- Promote individual medical care, for which purpose the officers of the companies included in the scope of this article shall:
- 1. Promote, in collaboration with the Superintendency of Public Health Campaigns (SUCAM MS), the training of employees for the performance of malaria and schistosomiasis prevention, diagnosis, and treatment activities and for vaccination against jungle yellow fever.
- 2. Install a small laboratory on the premises of the company for diagnosis of malaria and schistosomiasis in accordance with specifications provided by SUCAM MS.
- 3. Build, close to the laboratory, a dwelling properly covered with mosquito netting and having complete vertical walls, for malaria examination and treatment of patients.
- 4. Construct dwellings and houses which, even if rustic or temporary, have complete vertical walls on all sides; these should be situated in places well removed from pools of stagnant water or vector breeding grounds and be surrounded by an area with a radius of about 50 m having no vegetation.
- 5. Supply SUCAM/MS with detailed information on the routes of access roads to the area of the company, the annual program, the times at which clearing operations are carried out, the number of workers to be used, and their probable date of arrival at the worksite.

The Association of Amazonia Businessmen (AEA) signed an agreement with SUCAM with the aim of combating malaria at the site of agricultural projects. The following three clauses of the agreement are particularly worthy of note:

- 1. An AEA employee should be assigned to SUCAM to carry out the spraying and the epidemiological activities.
- 2. A small laboratory should be installed in the project area for malaria diagnosis.
- 3. Antimalaria drugs provided by SUCAM should be administered in all cases in accordance with the treatment scheme recommended by SUCAM.

(Source: Boletim Epidemiológico, 9(26), 1979. Ministry of Health of Brazil.)

Aedes aegypti Situation in Bolivia, 1980

In Bolivia. Aedes aegypti was found in 1980 in Santa Cruz Department in an area of approximately 85 km², which included the city of Santa Cruz and 45 adjacent localities. Along the navigable stretches of the Abuna and Mamoré rivers there were another 17 infested localities. The presence of the vector was also reported in Yacuiba, Todos Santos, and Puerto Suárez.

In 1943, Bolivia was the first country in the Americas to achieve A. aegypti eradication, after an intensive campaign. The country was officially declared to be free of the vector in 1948.

According to information from the National Epidemiology Division, A. aegypti surveillance was a responsibility of the Rural Endemic Disease Service from 1948 to 1957. In 1958, this responsibility was transferred to the National Malaria Eradication Service (SNEM). In 1966, the responsibility was again transferred, this time to the National Communicable Disease Institute (INET). In 1971 the surveillance program was reorganized as a result of a joint PAHO/WHO/INET study, and a plan was developed for A. aegypti surveillance throughout Bolivia. While sporadic surveys were made in some localities in Beni and Tarija. Santa Cruz Department, as well as systematic surveys at the international airport and railway terminal, surveillance activities at the national level were discontinued in October 1977.

On 7 February 1980, during field practices connected with a course on A. aegypti surveillance that was conducted in the city of Santa Cruz for the purpose of training personnel in entomologic surveys, A. aegypti larvae and adults were found and were identified by personnel participating in the course. The genus and species of the vector were subsequently confirmed at the Center for Tropical Diseases in Santa Cruz and in the laboratories of the Aedes aegypti regional eradication program in Bogotá, Colombia.

In view of the paucity of Ministry of Health resources at the local level, and in order to determine the area of dispersion of the vector, a survey was made around the area of El Trompillo international airport, where the first specimens of A. aegypti larvae and adults were found.

A small number of houses in alternate square blocks were inspected and the vector discovered in continuous areas from the airport to the center of the city and even in flower vases in the cathedral. No indices were taken, and therefore the density was not determined. According to information now available, only the city of Santa Cruz and two small nearby communities are infested. Of the 65 localities included in the surveillance plan, 27 have been surveyed. 24 of them with negative results (Figure 1).

Even though the source of the reinfestation cannot be precisely determined, it is believed that the A. aegypti might have been carried in airplanes from Cali, Colom-

bia, an infested city with which Santa Cruz has direct air communication, both for passengers and freight.

Emergency Activities

WHO and the neighboring countries were officially notified in accordance with the International Health Regulations as soon as the reinfestation was recognized, and the following activities were begun:

- The health authorities requested PAHO to provide technical advisers from 2-7 March to assist in assessing the situation arising from discovery of the A. aegypti reinfestation in Santa Cruz Department and in the planning of control and eradication activities.
- The health authorities declared the A. aegypti infestation to be a health emergency and developed a plan to be put into practice at the earliest possible time.
- The immediate objectives of the plan are control of the vector, reduction of its density, and prevention of its dissemination, in order to protect the population against the risk of an epidemic. For a second stage the target of the plan is final elimination of A. aegypti.
- Using existing resources in the Health Unit, and with the cooperation of airlines and ground transportation companies—buses as well as railways—all aircraft arriving at or departing from the airport, passenger and cargo planes alike, are to be fumigated in order to prevent the vector from spreading within Bolivia and into neighboring countries. Fumigation has also been decided upon for rail and bus terminals and at vehicle checkpoints or surveillance stations along the highways connecting the city with the rest of the country. Vector control activities were ordered to be instituted around the international airport, hospitals and other selected areas, along with the application of insecticide at ultra low volume (ULV) in the city of Santa Cruz, and with sanitation activities and the elimination of breeding grounds.
- In order to obtain complete information on infestation in the city of Santa Cruz, an entomologic survey was launched to provide a clearer picture of the distribution and density of the vector.
- Yellow fever vaccine is being administered collectively to people traveling to enzootic areas, as well as to international travellers bound for countries where a certificate of vaccination is required. At the surveillance station on the Yapacaní highway leading to the Ichilo area, which has a history of jungle yellow fever, vaccination will be compulsory. Health education, information, and community participation activities in support of emergency programs are being conducted with funds of the Health Unit.

(Biology and Vector Control Program, PAHO.)



Figure 1. Localities surveyed to determine the presence of Aedes aegypti. Bolivia. 1980.

- Localities with Aedes aegypti (surveyed)
- Localities without Aedes aegypti (surveyed)
- Capital of the country
- Capital of department
- International border
- -Interdepartmental line

Malaria Situation in Costa Rica, 1979

In 1979 the National Malaria Eradication Service examined 176.784 blood samples, of which 307 were found positive to the disease. Of these 274 were Plasmodium vivax, 31 were P. falciparum, 1 was combined P. vivax-P. falciparum, and 1 was P. malariae.

The provinces from which most cases were examined were Guanacaste, with 92 (30 per cent of the total), Puntarenas with 78 (25 per cent), and Alajuela with 32 (10.4 per cent). In San José Province, which is outside the malarious area, 69 cases (26 per cent of the total) were detected, most of them imported.

Of the total number of cases in 1978, 177 (58 per cent) were classified as imported: 140 came from Nicaragua. 23 from El Salvador, 12 from Honduras, and 2 from Guatemala.

More cases occurred in the consolidation area, mainly in the course of outbreaks, of which there was one of major importance in El Roble, Puntarenas, and adjacent areas, and another in Río Claro, in the southern Pacific coastal region.

During September and October, 8 cases were detected in El Roble and adjacent areas, 3 of which were imported from Nicaragua. In a second outbreak, which occurred in Rio Claro and four adjacent localities, there were 19 cases, all P. vivax.

Conditions during the rainy season favored an increase in the number of *Anopheles albimanus* breeding grounds. Transmission was attributed to this and to migratory movements, primarily from Nicaragua.

(Source: Semana Epidemiológica 8(10), 1980. Ministry of Health of Costa Rica.)

Recommendations Submitted During the Meeting on Yellow Fever in Belem, Brazil, 18-22 April 1980

Pathogenesis, Immunity and Diagnosis

In the event of a yellow fever epidemic, PAHO should develop protocols and organize a multidisciplinary team to conduct on-site investigations for the purpose of:

- Obtaining serial serum samples from patients as soon after onset of illness as possible and continuing through the acute phase of illness. Such samples are essential to the evaluation of rapid and early diagnostic techniques.
- Field testing the immunofluorescent antibody technique to determine its applicability for rapid diagnosis. To that end, investigations should be promoted to define optimal practical methods for preparing, storing, and shipping slides, and to determine viral strain and cell types to be used to inactivate the virulence.
- Collecting specimens that will allow direct comparison of cell cultures, in particular Aedes pseudoscutellaris (APo1), A. albopictus (C6/36), Vero, LLCMK₂, and others, with other methods including inoculation of mosquitoes and suckling mice, for isolation of yellow fever

virus and its identification by direct fluorescent antibody or complement-fixation tests.

• Conducting clinical studies on patients to define pathophysiologic features of the disease, including disseminated intravascular coagulation changes, acid-base and hemodynamic changes, possible immunopathologic mechanisms, endotoxemia, the occurrence of late myocardial and prolonged hepatic dysfunction, and the basis for acute renal failure (hepatorenal syndrome versus tubular necrosis).

PAHO should revise and update the manual on histopathologic diagnosis of yellow fever, considering atypical manifestations and lesions of other organs, and should distribute the revised version to laboratories and pathologists, as well as public health personnel.

Ecology and Epidemiology

PAHO encourages and supports ecological studies on yellow fever virus in areas where outbreaks periodically

occur. An effort should be made to determine if the virus persists in such areas during interepidemic periods and, if so, what the mechanisms of persistence are.

Vector Biology and Emergency Control

PAHO should take steps to strengthen its role in the elimination of Aedes aegypti in the Americas by:

- Updating continually its inventory of personnel, equipment, and insecticides available in national programs.
- Assisting in field and laboratory studies necessary to resolve problems associated with genetic makeup of A. aegypti strains and their vectoral capacity for yellow fever and dengue.
- Promoting research on the biology, ecology, population density, and geographic distribution of A. aegypti and of the jungle vector of yellow fever.
- Assisting in the determination of insecticide resistance in the Region.
- Preparing and distributing guidelines in vector biology and control.
- Encouraging practical training of pilots in aerial spray vector control technique.

Vaccine Supplies

PAHO/WHO should urgently undertake a long-term program directed at modernizing the yellow fever vaccine manufacturing capability in the Americas to meet expected increasing demands in volume and quality. The program should anticipate major investment requirements that will be critically needed within the coming decade. Program elements should include:

- An analysis by appropriate experts of present methods, potential future methods (e.g., cell culture), cost considerations, and requirements for developmental research. Such an analysis would require consultation with representatives of industry, national producers, national regulatory authorities, and international funding agencies. Guidelines should be prepared for the development of the next generation of yellow fever vaccines and production facilities.
- An advanced development program to elaborate and select improved methods for production of an inexpensive and safe vaccine equivalent or better in efficacy to the present product.

• The capitalization and construction of manufacturing facilities to meet the anticipated requirements.

PAHO should actively encourage and support research on new methods to characterize and standardize the existing 17D yellow fever vaccine and new methods for producing, stabilizing and administering it. Recommended research approaches include:

- Assuring stability of diluted vaccine and its improvement, and of lyophilized vaccine.
- Increasing the yield of virus from chicken embryonic pulp by washing the pulp once with diluent and using the wash for vaccine production.
- Improving lyophilization procedures, including nitrogen gas quality.
- Evaluating animal cell lines as virus production substrates, including animal and human cells, insect cells, and cultures in suspension.
- Evaluating further scratch vaccination methods and manufacture of this type of vaccine.
- Determining virus heterogeneity in molecular (oligonucleotide fingerprint, RNA complementation analysis) and other appropriate methods.
- Investigating alternative methods for detecting neurovirulence of vaccine seeds, including the neuroblastoma cell line.

The Scientific Advisory Committee on Dengue. Yellow Fever, and Aedes aegypti requested the Director of the Pan American Sanitary Bureau to convey to the Director of the Oswaldo Cruz Foundation. Rio de Janeiro, and the National Institute of Health. Bogotá, its great appreciation of the outstanding service rendered over the years by those two institutions in the production of yellow fever vaccine for the Americas.

The Committee further recommended that PAHO make available to both institutions sufficient resources to develop strong research programs in yellow fever vaccine formulation, production, testing, and delivery.

Likewise, it was recommended that the Newsletter on Dengue. Yellow Fever and Aedes aegypti be discontinued following a final issue, its purposes and programs to be included in the new PAHO Epidemiological Bulletin. The guide for surveillance of yellow fever, as devised by Dr. Groot and reviewed by Committee members, was recommended for publication in English and Spanish.

Report on Meetings and Seminars

Diarrheal Disease Control Workshop

Representatives of 15 English-speaking Caribbean countries and territories met in Kingston, Jamaica, 10-13 March 1980, to examine the problem of diarrheal diseases in the area and obtain additional information on the PAHO/WHO Diarrheal Disease Control Program. Specialized consultants and observers from PAHO, WHO, UNICEF, UNDP, and the Center for Disease Control (Atlanta, Georgia, United States) also attended.

The meeting included presentations on various aspects of diarrheal disease by authorities from the University of the West Indies (UWI), the Ministry of Health of Jamaica, the Caribbean Epidemiology Center (CAREC), and the Caribbean Food and Nutrition Institute (CFNI).

The topics examined included:

- Planning and administration of diarrheal disease control programs.
 - · Needs in the training field.
 - · Community organization and health education.
- Strategies for delivery of services in the framework of a diarrheal disease control program.
 - Epidemiological surveillance.

The group concluded that national diarrheal disease control programs should be developed and integrated within existing primary care systems in the Caribbean and should adopt the standards and guidelines established for the PAHO WHO Diarrheal Disease Control Program. It was pointed out that PAHO, UNICEF, CAREC, CFNI and UWI are in a position to provide technical cooperation for the establishment of national diarrheal disease control programs.

Finally, the group urged the Conference of Ministers Responsible for Health in the Caribbean to include the establishment of national diarrheal disease control programs on the agenda for its next meeting.

Copies of the final report of the workshop are available from PAHO upon request.

(Diarrheal Disease Prevention and Control Program, PAHO.)

Seminar on the Role of Laboratories in Epidemiological Surveillance against Communicable Diseases

This seminar was held in Lima, Peru, 3-7 March 1980, with the assistance of PAHO. The present epidemiology, laboratory, and health-statistics structures were reviewed with the aim of promoting their coordination in the organization of a communicable disease surveillance system in Peru. It was recommended that a committee be

established and a manual of standards and procedures be prepared for that purpose.

Inter-American Meeting, at the Ministerial Level, on Animal Health

This meeting took place in Washington, D.C., 14-17 April 1980. Two resolutions adopted at the meeting are especially worthy of note:

Rabies control and eradication

This resolution requests PAHO to give priority attention, within its programs of cooperation with the countries, to urban rabies and paralytic bovine rabies; recommends that the Pan American Zoonoses Center concentrate its efforts on and extend priority to the problem of rabies and expand its direct collaboration with the countries in the areas of diagnosis, biologicals production, epidemiology, and control systems, provided that the budgetary appropriation is sufficient for achieving those purposes; and urges countries with rabies problems to conduct national rabies control programs with a resolute decision to eradicate the disease.

Biologicals production and control

The delegates commended the Governments of El Salvador, Guatemala, Honduras, Mexico, and Panama for their initiative and work in the production and control of biologicals for veterinary use: requested the Director of the Pan American Sanitary Bureau to give his firm support to the structuring of a subregional program for production and control of biological products for veterinary use including Mexico, Central America and Panama; and reiterated the request to the United Nations Development Program for its financial support in implementing, as soon as possible, the regional program on production of veterinary biologicals and control of their quality, as well as for the necessary technical assistance.

Workshop on Diagnostic Techniques for Acute Viral Respiratory Diseases

This workshop was held 8-12 April 1980 at the Oswaldo Cruz Foundation in Rio de Janeiro, Brazil. The major part of the workshop, which was organized by PAHO and the Foundation, an agency of the Ministry of Health, was devoted to laboratory practices and demonstrations. The workshop was attended by laboratory professionals from Argentina, Bolivia, Brazil. Chile, Colombia, Ecuador, Jamaica, Mexico, Panama, Peru, Trinidad and Tobago, Uruguay, and Venezuela.

The group showed particular interest in taking part in the studies on the etiology of acute respiratory diseases to serve as the basis for control programs.

I Regional Seminar on Acute Respiratory Infections (ARIs)

The seminar took place in Rio de Janeiro, 12-13 April 1980. It was organized by PAHO's Division of Disease Prevention and Control and the National Public Health Pneumonology Division of Brazil. Discussions were held on epidemiological and clinical aspects and problems of major importance relating to ARIs. The seminar concluded with a symposium on the present situation and prospects for control of ARIs in Latin America. It was attended by professionals from Argentina, Chile, Colombia, Mexico, Venezuela, and various states of Brazil responsible for respiratory pathology control activities.

Recognizing the importance of acute respiratory infections as a public health problem, the participants recommended that:

- The Governments provide increased health care, beginning with young children.
- The program form part of primary health care, with an adequate referral system, standardized methods and techniques, and community participation, so that maximum coverage of the population may be achieved.
- Studies be made with a view to obtaining the necessary epidemiological, etiological, technical, and operational information for the planning, evaluation, and improvement of the program, concurrently with the conduct of activities.
- Diagnostic criteria and patterns of behavior vis-à-vis the patient be defined at each level.
- An exchange of information be instituted among the various countries and international organizations for the purpose of keeping abreast of information on ARIs.

Meeting of Experts to Prepare an ARI Research Protocol

The purpose of this meeting, held in Rio de Janeiro. 14-18 April 1980, with the collaboration of PAHO and WHO, was to prepare a protocol which, in addition to meeting the needs for information consistent with conditions in Brazil, could serve as a basis for similar studies in other countries of the Americas and regions of the world.

The organization of an ARI control program to reduce infant mortality, in which pneumonia is the primary cause, requires epidemiological, technical, and operational information so that standards can be developed, personnel trained, requirements programmed, and results evaluated.

V International Conference on the Mycoses

This conference, held in Caracas, Venezuela, 27-30 April, dealt with the subject of superficial and subcutaneous mycoses. It was organized and sponsored by the Government of Venezuela and PAHO and attended by 60 participants and some 40 observers from the Americas and Spain.

This conference was the fifth in a series that started in 1970 and whose purpose is to review specific aspects of the subject. Previous meetings dealt with: public health. diagnostic. therapeutic. epidemiologic. and training aspects (Washington, D.C., 1970); paracoccidioidomycosis (Medellín, Colombia, 1971); immunity and pathogenic mechanisms, laboratory aspects, opportunistic mycosis, and chemotherapeutic agents (São Paulo, Brazil, 1974); and white and black yeasts (Brasília, 1977). The papers presented at those conferences have been published by PAHO in its Scientific Publications series.

Calendar of Meetings and Courses

Central American Course on General Epidemiology. San José. Costa Rica, 26-30 May 1980

National participants and students from other countries are to attend this course, which was organized by the University of Costa Rica School of Medicine, the Community Health Training Program of Central America and Panama (PASCCAP), and PAHO.

Seminar on Epidemiological Surveillance of Rabies. Lima. Peru, 9 June 1980

The objective of this seminar is to review and update the rabies control procedures used in the various regions of the country.

Course on Methodology for Epidemiological Research. Mexico City. 16 June 1980

Annual Workshop of the Collaborative Treatment Research Program.

Bogotá, Colombia, 17-21 June 1980

The aim of this workshop is to examine progress under the treatment research protocol used in the program. The workshop also includes discussion of the latest advances in the treatment of cancer, future collaborative activities in this field, and expansion of the program to include radiotherapy and the epidemiological research project.

Operation and Maintenance of Equipment and Insecticide Application Techniques.

Cali. Colombia. 7-18 July 1980

Information on the operation and maintenance of modern insecticide application equipment is to be disseminated at this event, which is to include practice in its operation, calibration, and repair.

Study Group on Immunology Problems in Rabies. Washington, D.C., 10-11 July 1980

Representatives of the Wistar Institute and United States and Latin American technicians are to participate in this meeting. Its objective is to study problems arising in rabies vaccination when immunologic differences are found to exist between the viruses used in producing the vaccine and those existing in the field. A work protocol is to be drawn up for application in six Latin American laboratories.

Seminar on Brucellosis and Anthrax. Huacho, Peru. 18-22 August 1980

The aims of this seminar are to discuss the strategy used in this field, evaluate the results of the brucellosis control program, update the existing knowledge of anthrax, and establish control procedures.

International Course on Clinical Epidemiology.

McMaster University, Hamilton, Ontario, Canada, JulyDecember 1981

With funding from the Rockefeller Foundation, Mc-Master University will offer an intensive course in clinical epidemiology for junior faculty members in clinical departments of medical schools in developing countries. The course will include concepts, principles, methods, and practical applications of epidemiology. Two months will be devoted to the basic concepts of causation, bias, clinical measurement, natural history, and disease frequency. In the four following months the participants will be familiarized with advanced skills in the areas of design, research problems, sampling, maneuvers, measurements, events, and analyses.

Enrollment will be limited to eight students per year. Financial support covers tuition, travel, and maintenance expenses of the recipient. After a student has successfully completed the course, modest research support will be provided to the participant's home institution and for a visit by the preceptor to that institution to consult on the research project.

Applications should be submitted in a letter specifying the candidate's experience, interests, present position, and future plans. A curriculum vitae should be attached, and also letters of recommendation from the applicant's department head and dean stating their reasons for supporting the application. Preference will be given to candidates with assured appointments in departments of internal and family medicine, but those from other clinical departments are not precluded. The closing date for receipt of applications is 1 November 1980; decisions will be announced by 15 January 1981. All correspondence should be addressed to: Peter Tugwell, M.D., Chairman, Department of Clinical Epidemiology and Biostatistics, McMaster University, 1200 Main Street West, Hamilton, L8S 4J9, Canada. Telephone: (416) 525-9146.

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