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**PAN AMERICAN HEALTH ORGANIZATION**

**ADVISORY COMMITTEE  
ON MEDICAL RESEARCH.**

**FIFTEENTH MEETING  
13-17 JUNE 1976  
BRASÍLIA, D.F., BRAZIL**

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**REPORT TO THE DIRECTOR**

Ref: RD 15/5

10 July 1976

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

WASHINGTON, D.C.

REPORT TO THE DIRECTOR

Advisory Committee on Medical Research  
Pan American Health Organization

Fifteenth Meeting    13-17 June 1976    Brasília, D.F., Brazil

PAN AMERICAN HEALTH ORGANIZATION  
WASHINGTON, D.C.

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## PAHO ADVISORY COMMITTEE ON MEDICAL RESEARCH

Report to the Director

1976

### Introduction

The Fifteenth Meeting of the Pan American Health Organization's Advisory Committee on Medical Research, held in the PAHO building at Brasília, D.F., Brazil, from 13 to 17 June 1976, was called to order by the Chairman, Professor John C. Waterlow. The Director of PAHO, Dr. Héctor R. Acuña, greeted the new members of the Committee: Dr. Joaquín Cravioto, Chairman, Department of Research, Children's Bureau of Mexico; Dr. Pedro Galindo, Director, Gorgas Memorial Laboratory, Panama; Dr. Luis Leloir, Director, Institute of Biochemical Research, Argentina; Dr. Fernando Monckeberg, Director, Laboratory of Pediatric Research, University of Chile; Dr. Daniel Okun, Chairman, Department of Environmental Engineering, School of Public Health, University of North Carolina; and regretted the absence of Dr. G. Malcolm Brown, Sir Ernst Chain, Dr. Donald Fredrickson, Dr. Miguel Layrisse, and Dr. Guillermo Soberón. He noted with pleasure the presence of Dr. Leon Jacobs, of the National Institutes of Health, representing that agency at the meeting of the Committee.

The Director expressed his honor at having the Minister of Health of Brazil, Dr. Paulo de Almeida Machado, preside over the inaugural session, and his appreciation for the Government of Brazil's generous assistance in bringing the meeting to that country.

The Director called attention to the fact that it was the first time the ACMR was convened outside of PAHO's Headquarters in Washington, D.C. He suggested that future meetings of the Committee be alternately scheduled in

Washington, D.C., and other member countries of PAHO. The rotation of the meeting to other countries would thus, in time, insure balanced geographic representation of research projects that the Committee would review in situ. The Director praised the efforts of the Government of Brazil to support research and scientific manpower development.

In concluding, the Director recommended that the Committee elect a Chairman for the next 3 years, and that the elected Chairman report on the Committee's activities to the XXIV Meeting of the PAHO Directing Council, to be held in Mexico City from 27 September to 8 October 1976.

The Minister of Health of Brazil, Dr. Paulo de Almeida Machado, then extended the hospitality of his Government to the invited scientists and acknowledged the endeavors of the Pan American Health Organization to support and coordinate health research activities in the Western Hemisphere.

The Minister referred to Brazil's Second Three-Year Plan for the Development of Science and Technology and expressed the hope that the information and discussions arising from the Committee's meeting would contribute to the furtherance of the Plan's health research goals.

The meeting's agenda was undertaken the following day, beginning with the presentation of the topics that follow, and ending with an executive session of the PAHO/ACMR. Dr. George O. Alleyne was the appointed Rapporteur for the meeting.

#### 1. Research in Progress 1976

The 15-year old PAHO research program has progressed from a modest beginning to an investment of approximately five million dollars a year on research and research training schemes in a wide variety of subjects relevant to health problems in the Americas. Although funds come mainly from sources outside the Organization's regular budget, PAHO plays an important catalytic function in securing this support and in identifying projects that can effectively use it. Research in Progress 1976 summarizes 151 projects--ranging from basic laboratory research, to clinical, epidemiologic, and methodologic studies--in which PAHO participates as grantor,

grantee, or collaborator. The publication is not intended to be an exhaustive, detailed, scientific report of each project, but rather a summary statement of the problems, methods, results to date, and significance of a study under way. Often times the project listed is only at the beginning stage and no results are yet available. In the 15 years of its operation, the program has focused on: (1) stimulation and support of biomedical research and research training with emphasis on collaborative multinational projects; (2) strengthening of biomedical communications and resources through scientific meetings and the provision of modern bibliographic and other library services; and (3) promotion and application of operations research to improve the efficiency of health facilities and programs.

The early meetings of the Advisory Committee on Medical Research were devoted to a systematic review of needs and opportunities for research of practically all fields in which PAHO had a program commitment. The Committee was then concerned with obtaining answers to such questions as: What was the present state of knowledge in the field? What were the areas of ignorance? What current research--particularly in Latin America and the Caribbean--attempted to fill the gaps of knowledge? Who was doing it, where, and how adequately? What complementary efforts were needed--particularly from an international agency such as PAHO--to strengthen or accelerate the ongoing studies, and what new research should be encouraged or initiated? In this exercise, large numbers of experts--including members of the ACMR--were used as single consultants, members of PAHO scientific advisory groups, or participants in scientific meetings and symposia sponsored by the Organization. In either case, the consultants visited--or had firsthand knowledge of--the institutions, investigators, or research projects they were asked to evaluate. This continuing activity has resulted in the publication of 216 technical reports and 31 scientific monographs. Within the constraints of limited research funds from PAHO's regular budget or obtained from outside sources, the Organization has made a sustained effort to implement the recommendations of the consultants, after, of course, appropriate scrutiny and endorsement by the Committee. Examples of major direct accomplishments of the research program in the past 15 years are

the Regional Library of Medicine and the Health Sciences in São Paulo; the Caribbean Epidemiology Centre in Port of Spain; the two Immunology Research and Training Centers in São Paulo and Mexico City; the PAHO/Walter Reed/Instituto Evandro Chagas Research Unit on disease surveillance in Belém; the PAHO/Harvard/Wellcome/University of Bahia Research Unit on Chagas' disease and schistosomiasis in Salvador; the Perinatology Center in Montevideo; the special research programs on endemic goiter, mycology, arbovirology, and dengue; the grants program for research and research training; and the program of scientific meetings and symposia whose proceedings are recorded in the PAHO scientific publication series. Some of these activities are described in Research in Progress 1976 (Document RD 15/1).

The criticism has sometimes been made that the PAHO research program lacks balance in its support of the different health problem areas and that some of the areas receiving support--such as nutrition--are relatively overfunded. It should be recalled, however, that in the absence of substantial, uncommitted, regularly budgeted PAHO research funds, the only way to have a significant program in these 15 years was to attempt to marry the research priorities of the Organization to those of granting agencies. This "match-making" effort has been rather successful, and the resulting program not too different from the ideal one PAHO would have, if it were to pay for it in full.

*In discussing the progress report, the Committee noted that the PAHO budget for research was approximately 5 million dollars and that the Organization contributed approximately 30 percent of the costs of the projects listed as being supported by PAHO. It was stressed that whereas previously there had been a strong emphasis on nutrition, there was now an additional need for operational research in several areas. Since approximately 70-80 percent of the work supported by PAHO is done in centers, institutes, and universities, PAHO should insure that its centers develop close relationships with the local scientific communities and should also try to be involved in graduate education. It was noted that some of the PAHO centers did play these roles. PAHO also contributed*

to research not based on centers by providing training, catalyzing the initiation of projects, and funding individual investigators when necessary.

It was also agreed that the written report of the directors of PAHO Centers should be circulated to the Committee annually. Some of these points are discussed more extensively in the report on the Executive Session (see item 22, page 36).

The suggestion was made that future issues of the volume Research in Progress might include, in a supplemental document to be distributed to ACMR members only, an executive summary prepared by the Secretary with the help of one or several Committee members, which would outline the questions being addressed in several research categories, their relations to the five priorities given in item 22 of this Report, a determination of what aspects of a particular research might be emphasized or discontinued, and specific recommendations for the Committee's consideration.

## 2. The PAHO/Harvard/Wellcome/UFBa/INERu Project

The background of support and the development of the project were reviewed. In 1970 the Trustees of the Wellcome Trust made an annual grant of £50,000 to the Department of Tropical Public Health at Harvard for a 10-year period. The objective was to support the training and development of young scientists working overseas in the area of tropical medicine.

It was decided from the start that the subject of the studies would be determined by the interests of the trainee. A second decision was that a truly collaborative and mutually profitable relationship would need to be established within an existing biomedical academic center to house a base laboratory.

The initial trainees chose to work on Chagas' disease and on schistosomiasis, so, for logistical reasons, it was necessary to find an appropriate site where both diseases were endemic.

A survey indicated that an ideal arrangement could be developed at the Federal University of Bahia in Salvador. Laboratory space was provided through the courtesy of the Rector of that University and facilities became functional in July 1973. Access to a rural population in an area--Castro Alves--where both diseases are highly endemic was facilitated by the staff of the Instituto de Endemias Rurais-Fundação Instituto Oswaldo Cruz (INERu-FIOCRUZ). PAHO provided the essential laboratory equipment and invaluable logistical support. More recently, a Brazilian trainee has been financed by the Industria e Comercio de Minerios (ICOMI). Thus the project has many sponsors and has developed into a collaborative activity involving many scientific disciplines and agencies.

Three reports were then presented describing results obtained so far.

### 3. Epidemiologic Studies on Chagas' Disease; Clinical and Serological Correlations

A high prevalence of seropositivity to Trypanosoma cruzi as detected by the complement fixation (CF) and the indirect immunofluorescence (IF) tests was found in a rural population in northeastern Brazil. The prevalence increased gradually in groups up to age 20, remained about 60 percent through age 55 and gradually declined in older age groups. Geometric mean titers of the CF and IF tests showed little variation between groups over the age of 25.

Clustering of seropositivity in households was found and the presence of a seropositive child less than 10 years of age was a useful index of a high rate of seropositivity in that household.

Atrioventricular conduction defects, ventricular conduction defects, and arrhythmias (Sections 6, 7, and 8 of the Minnesota Code) were 6 times more frequent among persons with seropositive reactions than among those with seronegative ones. Seropositive males between the ages of 25 to 44 had 8 times the frequency of arrhythmias and conduction defects as the seronegative group. Seropositive individuals with ventricular conduction

defects had a median age which was 15 years less than the age of individuals with ventricular ectopic activity alone or in combination with ventricular conduction defects.

No clustering of electrocardiographic abnormalities was found in households beyond that expected by the distribution of seropositivity in houses. House construction, presence of Panstrongylus megistus, or the age of the youngest seropositive child did not increase clustering of ECG abnormalities. These data do not support the theory that reinfection is important in the pathogenesis of Chagas' disease cardiomyopathy.

In well-constructed mud brick houses in this rural area, all children under the age of 10 were seronegative. In contrast, in unplastered mud stick houses, children in that age group had a seropositivity rate 2.6 times that of children in plastered mud stick houses. With increasing density of P. megistus in houses, among which at least one was positive for T. cruzi, there was a proportional increase in seropositivity in the household.

#### 4. Serological and Cultural Studies on Patients With Chronic Chagas' Disease; Evidence of CNS Involvement in the Acute Phase

The complement fixation (CF) and the indirect immunofluorescence (IF) tests for T. cruzi infection were evaluated and found to be reproducible and reliable for epidemiological studies. The concordance between the two tests was 96 percent in the Castro Alves study.

In a study of patients hospitalized with a presumptive diagnosis of chronic Chagas' disease cardiomyopathy, 22 of 25 patients were seropositive by the CF and IF tests. T. cruzi was detected either by xenodiagnosis or blood culture in 11 of 22 (50 percent) seropositive patients. Blood culture was more sensitive than xenodiagnosis with 10 Triatoma infestans. Preculture concentration of the parasites in blood by the  $\text{NH}_4\text{Cl}$  hemolysis-centrifugation technique doubled the isolation efficiency of blood culture. Persistent T. cruzi parasitemia seemed to be characteristic of chronic Chagas' disease cardiomyopathy.



T. cruzi was detected in the cerebrospinal fluid (CSF) of seven of nine patients with acute Chagas' disease. Presence of T. cruzi in the CSF was not accompanied by any detectable cytologic or biochemical changes except for slight elevation of IgG. Anti-T. cruzi antibodies were present in the serum but were not detected in the CSF. Parasitization of the CNS by T. cruzi in acute Chagas' disease indicates the need for investigating subsequent neurologic or mental disorders in chronic infection.

In the northeastern Amaralina District of the City of Salvador, 120 (14.0 percent) of 856 pregnant women were found to be seropositive for T. cruzi infection. T. cruzi was detected in the cord blood of 1 of 17 placentas obtained from seropositive women. The offspring from this case were premature twins who died during the neonatal period. T. cruzi was detected in their peripheral blood before death and in their tissues at autopsy. Cord blood serum tested by IF was positive for IgG antibodies but not for IgM antibodies. In a familial investigation of this case, T. cruzi was demonstrated in the mother, who was born in the interior, and in three of her five living children, who were all born in the city of Salvador. The mother also had one pregnancy that ended with a premature stillborn fetus. In absence of evidence for triatome transmission, T. cruzi infection of her other three children may also have been congenitally acquired.

*The Committee was impressed with the amount of work which had been produced on this important topic in the short time that the project has been operational. It was pointed out that many of the aspects of Chagas' disease which were now being evidenced, such as spastic neuropathy, had been described by Chagas in 1909. There was discussion on the possibility that there were marked differences in the expressions and sequelae of the disease in different countries. Whereas parasitism once acquired appeared to be permanent in Brazil, there were well-documented cases from Panama showing that the parasitism could disappear. The possibility was also raised that Chagas' disease had not always been a human infection throughout Latin America, but that there had been a change in the infectivity of the trypanosome. There was also no firm information on whether*

cardiovascular disease resulted from a series of reinfections or whether a single infection was all that was necessary.

The Committee attached so much importance to the issues raised by these studies and unanswered questions that a subcommittee comprising Drs. Chagas, Weller, Sabin, and Galindo was appointed to examine the priorities in relation to research on Chagas' disease, with special reference to the recommendations arising from the scientific meeting held in Belo Horizonte in March 1975 (PAHO Scientific Publication No. 318).

The subcommittee accepted that Chagas' disease research can be pursued along two main lines: epidemiologic research aimed at determining the actual morbidity and mortality of the disease in relation to prevalence of infection; and basic studies, many of which were covered at the Belo Horizonte meeting. In addition, it was recommended that countries, within their own set of priorities, should set up task forces to determine the magnitude of the disease problem in different areas of Latin America.

##### 5. Intensity and Effects of Schistosoma mansoni Infections in a Rural Community in Northeastern Brazil

The intensity of infection with Schistosoma mansoni and its effects were investigated in a defined population living on three contiguous "fazendas" (subcounties) in a nonmalarious area of northeastern Brazil near Salvador, Bahia. Quantitative stool egg counts (Bell technique) were performed on 363 of 417 individuals (90 percent) of all ages; physical examinations were done on 294 of 357 persons (82 percent) 5 years of age and older. The maximum increase in prevalence was observed between the 1 to 4- and 5 to 9-year age groups, while the maximum increase in fecal egg count occurred between the 5 to 9- and 10 to 14-year age groups. Highest egg counts were observed in the 10 to 14-year age group (geometric mean of 301 eggs per milliliter of stool) while the maximum prevalence (100 percent) was in the 20 to 24-year age group. In the "fazenda" with the lowest quantitative egg counts the age specific prevalence rates increased more slowly than in the "fazendas" with higher egg counts. In the study, nearly 50 percent of the total fecal egg output was accounted

for by 22 individuals (6 percent) who had a mean age of 12.6 years. Egg counts for this selected group were all over 800 eggs per ml of stool with a mean of 1,514 eggs per ml stool. In children under 15 years of age, the frequency of hepatomegaly and splenomegaly varied directly with the egg count; further, the degree of hepatomegaly was directly correlated with increasing egg counts. No splenic enlargement was noted in children not excreting eggs. In adults, on the other hand, neither splenomegaly nor hepatomegaly could be directly related to schistosomal infection per se. In children neither the presence of infection with S. mansoni nor its intensity was reflected by altered anthropometric measurements. In the one "fazenda" tested, the frequency of stools positive for occult blood correlated with increasing S. mansoni egg counts.

*The Committee expressed interest in this work, which provides data bearing on the development of strategies or approaches to control this disease. This study has highlighted some of the questions that needed to be answered in research on schistosomiasis. There was no clear indication that nutritional status affected the severity or expressions of the disease. It was not clear that hepatomegaly or splenomegaly in themselves were associated with clinical disease caused by schistosomiasis. Was the decision to treat the acute cases in children based on a concern for eventual clinical sequelae or an attempt to stop the excretion of eggs? The answers to many of these questions lie in good longitudinal studies. In view of the information that was presented, it was agreed that a strategy should be developed to determine the magnitude of the disease problem caused by schistosomiasis.*

6. Studies on the Immunopathogenesis of Rheumatic Fever and Acute Glomerulonephritis in Trinidad

A number of reports have demonstrated that the incidence of streptococcal infections and their sequelae, namely rheumatic fever and glomerulonephritis, is high on the island of Trinidad. Recent studies have shown that the prevalence rate of streptococcal infections of the skin and throat is unusually high in the island. Approximately every 4-5 years there has

been a serious epidemic outbreak of nephritis, caused by nephritogenic strains of streptococci whose portal of entry is the skin, usually as a result of bites of mosquitoes or, in some instances, outbreaks of scabies. In the past, three major types of Group A streptococci have been responsible for these outbreaks, namely, Type 49, Type 55, and Type 56 streptococci. As many as 1,000 cases of acute poststreptococcal glomerulonephritis have been seen during the course of these epidemics.

Equally important has been the incidence of rheumatic fever. Though Group A streptococci have been isolated from the throats of only a small (15-20) percent of these patients, it appears that the type of strain responsible for the induction of rheumatic fever is different from that causing streptococcal glomerulonephritis. Approximately 300-400 cases of acute rheumatic fever are seen each year on the island, and a significant proportion of them are probably recurrences of this disease. The simultaneous occurrence of the two diseases side by side in the same relatively closed population provided a unique opportunity to study the cellular and humoral immune response in both disease states.

Patients were studied either at the Port of Spain General Hospital or the San Fernando General Hospital. The average age for the acute rheumatic fever group was 6-8 years, and the acute glomerulonephritis group was usually 3-4 years of age.

The migration of peripheral blood leukocytes from capillary tubes in the presence of antigen and blast transformation of peripheral blood lymphocytes were used as indices of cellular reactivity to a given antigen. A significant degree of cellular reactivity to streptococcal antigens was found in rheumatic versus nonrheumatic individuals, both with isolated Group A streptococcal cell walls and membranes. This seemed to be specific for the strains studied, in that rheumatics reacted unusually only to the throat strains and not to the skin strains tested. However, a comparison of reactions of rheumatics to those of nephritics with these same antigens, showed no significant difference between the two groups. Similar results were found in the studies on blast transformation: nephritics and rheumatics did not seem to be different with respect to the strains studied. An

interesting finding was that there appeared to be a decreased frequency of HL-A5 in nephritic and rheumatic patients.

One interpretation is that there is a possible unusual cellular reactivity to certain Group A streptococcal strains in rheumatic individuals, but, unless more purified antigens are used, the general level of streptococcal reactivity in both rheumatics and nephritics is so high that subtle differences will not be picked up with the antigen preparation.

*The Committee discussed this work, its public health importance, and the desirability of extending it to cover the aspect of dental infection with streptococci. It was pointed out that only a very small proportion of persons who had streptococcal infections ever progressed to clinically apparent disease and the present work might eventually help to identify the persons with heightened cellular reactivity to streptococcal antigens before they acquire nephritis or rheumatic fever. It might then be possible to initiate proper methods of protection perhaps by vaccine. The Committee noted that investigations such as the ones just described served as a good example of the interaction of basic and community-oriented research.*

#### 7. Rabies and the Ecology of the Mongoose in Grenada

An investigation into the role of the mongoose (Herpestes auro-punctatus) in causing rabies in Grenada was undertaken between 1968 and 1975 under a joint Government of Grenada/U.K. Medical Research Council/Pan American Health Organization project. The extent of the problem was shown by the fact that four persons died of rabies in Grenada from 1968 to 1975; antirabies treatment was given to 22.8 cases per year in average, and 56 percent of all the cases treated had been bitten by mongooses. A total of 97 livestock was reported rabid during the study period between 1968 and 1975, and rabies was diagnosed in 32 dogs and 12 cats. Bats were the only other wildlife species in which rabies was diagnosed.

The study confirmed the importance of the mongoose as a reservoir for rabies. There was a fluctuation in the prevalence of rabies in the mongoose since the rabid animals as a percentage of the total trapped

varied from 3.7 percent in 1968 to 0.5 percent in 1970. Nevertheless a total of 475 rabid mongooses was found during the period of study. The presence of rabies in mongooses was also established by finding neutralizing antibody against rabies in 29.7 percent of all the 1,675 mongooses tested. Significant titers of antibody were found in 8 percent of 352 bats examined.

Mongooses were found throughout Grenada and population estimates varied from 1.3 to 4.2 animals per acre. Data were obtained on the movements of the animals, litter size, adult weights, and sex ratio. It seems that it is impossible to eradicate the mongoose population and containment is the best that can be expected.

*The Committee discussed the problem of rabies in regard also to its appearance in and gradual spread across Europe. It was noted that the presence of a reservoir of rabies did not always lead to human rabies, and in Trinidad there were rabid vampire bats but no human rabies. The difficulties in providing an effective vaccine against mongoose rabies were stressed. The question of the protection of an oral vaccine against rabies was discussed.*

#### 8. Spirochetal Infection in Isolated Indian Populations

There has been concern over the effect of venereal infections on Brazilian Indians who have been contacted recently. Grossly divergent treponemal antibody patterns have been found in different Brazilian Indian tribes. The VDRL and FTA-ABS tests have been used. No positive reactions were found in the recently contacted Paracanan; a few positive reactions were noted in the Tiriyo about 15 years after first innocuous contact; but very high reaction rates were found in three Kayapó groups, the Kuben Kran Kegn, Xikrin, and Mekranoti, who had had intermittent contact with outsiders. The Kayapó incidence was higher than in a comparable sample of specimens collected in Tahiti at the time and place of a major epidemic.

Pinta has been reported among the Kuben Kran Kegn but careful examination of every member of the other two Kayapó tribes has revealed

no sign of pinta, no congenital or venereal syphilis, and no significant evidence of yaws.

In the study reported, the youngest person with the more specific FTA antibody was 9 years old. The incidence increased through the young adult group, suggesting acquisition contemporary with sexual activity. There was no mother-child or husband-wife association. The positive reactions were not associated with reactions against *Leptospira* or *Borrelia*, indicating that they had not been elicited by these other spirochetes. Only 2 percent of the sera were positive for gonococcal pili antigen, suggesting that the infection was not attributable to frequent contact with outsiders. Paired specimens collected 2 1/2 years apart indicated a large number of conversions in the Mekranoti, but few in the Xikrin.

It seems possible that certain tribes have a high incidence of infection with treponema which, either because of the spirochetal or the human genetic constitution, causes very little morbidity.

*The Committee considered the possibility that the tribes had not been as isolated as had previously been supposed and there was evidence that there had been definite but episodic contact between Brazilian settlers and Indians. It was suggested that anthropological studies might contribute evidence for disease in the populations being studied. The Committee heard that in spite of the occurrence of treponemal antibodies in the blood, there was no clinical evidence of tertiary syphilis although it was stressed that investigators may have to look for manifestations other than those which have been usually found in other societies.*

*The Committee expressed interest in this work, especially in the possibility of interdisciplinary collaboration.*

#### 9. Investigation of an Outbreak of Encephalitis in the State of São Paulo

An outbreak of human encephalitis occurred in the counties of Itanhaem, Peruíbe, and Mongaguá in the State of São Paulo, south of Santos. The epidemic region is about 1,000 km<sup>2</sup> and is a flat coastal area limited by the Serra do Mar mountain range. The average temperature is of 21°C with an annual rainfall

of about 2,000 mm. The economy of the region is based on tourism and banana culture.

The epidemic began abruptly in March 1975 and lasted till the end of June. A total of 465 cases was observed. With few exceptions, they were all from rural areas. In September 1975, the epidemic spread to Iguape, a neighboring county and 52 cases with 5 deaths were reported.

The clinical picture was similar to that of St. Louis encephalitis or Japanese B encephalitis: fever, headache, tremors, muscular weakness, and in some severe cases, lethargic coma. Cerebrospinal fluid examinations showed about 500 cells per mm<sup>3</sup>, predominantly lymphocytes.

Serological tests with four flavivirus antigens (yellow fever, Ilheus, St. Louis encephalitis, and Bussuquara) indicated that in 195 of 230 paired sera (85 percent) there was evidence that the illness was related to an increase in antibodies to flaviviruses. A virus, isolated at post-mortem examination of a patient from Iguape, appeared to be a new member of the flavivirus group, antigenically distinct from any other known arboviruses. It seemed to be responsible for the outbreak of encephalitis, as judged by the patient's serological response.

The attack rate was very high (4.4 percent). Adult males were more affected than women, but children of either sex were affected almost identically. Mortality was deeply influenced by hospital care.

The main vector remains to be discovered and man does not seem to have any essential part in the maintenance of the virus in nature. Judging by the high attack rate, and by the fact that adults are more attacked than children and that the disease was not previously known by local inhabitants, it appears that the virus has recently been introduced in the region or has been introduced in a specially virulent form.

In January 1975, several cases were seen in Cananeia, south of the epidemic area. It would thus appear that there is an epidemic wave of this flavivirus agent, which is a potential menace to other states in southern Brazil and to neighboring countries.



The Committee received this work with interest and suggested that:

1. The Pan American Health Organization advise the Health Ministry of Brazil of the importance of giving the utmost priority to more extensive studies on the virology, epidemiology, and ecology of the flavivirus isolated by Dr. Oscar Souza Lopez, of the Adolfo Lutz Institute of São Paulo, in order to elucidate the reservoir and vector-host relationships of this potentially dangerous arbovirus.

It recommended that the first and highest priority be given to a carefully planned serologic survey of:

- (a) human beings of different ages and
- (b) certain birds and animals, using one of the strains of the new virus for the optimum neutralization test. The regions to be surveyed should include not only different rural and urban areas of the State of São Paulo, but also other selected areas of Brazil and of the Western Hemisphere. This serologic survey should indicate whether a new virus is involved which has not previously infected human beings and/or animals in São Paulo and elsewhere in Brazil or whether it is a specially virulent strain of a virus that has previously infected human beings without causing recognizable disease.

Future strategy would be greatly influenced by this preliminary information. This task will require considerable increase in staff and facilities.

2. The Pan American Health Organization request the Center for Disease Control of the U.S. Public Health Service to prepare sufficient amounts of specific neutralizing antiserum of this flavivirus, and to make it available to virological laboratories in member countries, particularly in Mexico, Central America, Panama, Ecuador, Colombia, Venezuela, and Trinidad, in order to allow the establishment of proper surveillance mechanisms for the early detection of this arbovirus.

10. Foot-and-Mouth Disease: Route of Immunization in Relation to Control Programs

The impact of foot-and-mouth disease (FMD) on economy is notable as it interferes with world trade in livestock and livestock products and can result in the closing of markets badly needed by several South American countries. The disease causes decreased milk production, weight loss, and abortions in cattle, and direct losses to the economy of a country. Livestock mortality is usually not high except in young pigs or lambs but the after-effects of the disease can be serious: cattle often grow very slowly and become poor producers.

FMD is an acute, highly communicable disease caused by a picorna-virus with a large number of immunologic types and subtypes affecting a wide range of cloven-hoofed animals--cattle, pigs, sheep, goats, llama, and wild species such as deer. Because presently used inactivated vaccines give a protection of relatively short duration, cattle in many areas are being vaccinated as often as 3 times a year. A good-quality vaccine can induce adequate levels of circulating antibody, but provides little or no protection against virus multiplication in the upper respiratory tract. Thus, although vaccination programs prevent a great deal of physical losses, they may not be effective in breaking the transmission chain of the virus.

Convincing evidence is accumulating that FMD virus spreads by aerosols generated by infected livestock. It was also shown that local defense and/or immune recall mechanisms may be at least as important as the circulating neutralizing antibodies for protection of the animal. Thus, in terms of resistance, not only must the preexposure virus-neutralizing antibody titers be considered, but also the rapidity and intensity of the immune response upon infection.

Subtype or strain differences occur quite frequently because of the ease with which FMD virus undergoes subtle changes in its antigenic structure, thus circumventing the population immunity. Moreover, vaccine production methods may favor an antigenic component that deviates from the field strains as sometimes has happened with virus cultured in cell suspension. Therefore,

it is important to keep track of the characteristics of the field viruses and of viruses being used for vaccine production. It is also important to make vaccines with a wide immunogenic coverage and of such high potency that they provide reasonable protection even against somewhat distinct variants or strains. The use of mineral oil as a vaccine adjuvant has given very promising results in producing higher and longer lasting levels of immunity.

The overall lack of success of modified live FMD virus vaccines may be traced back to an excessive emphasis on systemic immunity and to the intramuscular or subcutaneous route of application. Intranasal vaccination should be considered to activate the local defense mechanisms and to interfere with the transmission of the wild virus.

*The Committee accepted that researchers must continue to improve the systems of vaccine production and control, to guarantee adequate supplies of innocuous vaccines of high potency.*

*In discussion it was pointed out that the vaccine protected against the disease and not against the acquisition of the infection. Attention was drawn to the failure of nasally administered influenza vaccine to control influenza in humans. The Committee felt, however, that there should be an expanded program to find an effective vaccine and that the Director of the Pan American Foot-and-Mouth Disease Center should be requested to present proposals with a budget for the development of a live attenuated vaccine for FMD.*

#### 11. The Armadillo as a Laboratory Animal

A brief bibliographic review on the use of the armadillo, with special reference to Dasyus novemcinctus (nine-banded armadillo of New Mexico) in biomedical research shows the importance of this experimental model in such areas as embryology, genetics, teratology, organ transplantation, immunology, and infectious diseases. Scientific attention has been focused on the armadillo since its use in the experimental reproduction of leprosy.

Dasyus hybridus (seven-banded armadillo) and Chaetophractus villosus have been studied with a view to contributing to the knowledge of the biological constants and the natural pathology of the different species of armadillos.

The histologic structure of several segments of the skin, lymph nodes, spleen, and thymus were described. A complete hematologic profile was established with data from 26 armadillos (10 males and 16 females). The body temperature levels of D. hybridus were also recorded.

Interstitial nephritis in Chaetophractus villosus was shown to be caused by leptospirae. Results of the serologic and bacteriologic examination of the sera of 89 armadillos showed that 16 (17.9 percent) had agglutinin titers of 1:100 or higher for leptospirosis with a predominance of the Hebdomadis group and serotypes bataviae and canicola. Histopathologic study showed an interstitial nephritis in 11 of the 13 animals examined. The remaining 2, which had no evidence of lesions, were the animals in which the Leptospira biflexa strain (nonpathogenic) was isolated.

*The Committee expressed interest in the development of this new species of laboratory animal, especially in view of its importance for the study of the mycobacteria. Efforts were being made to breed the animals in captivity and develop colonies with well-established characteristics. It would then be possible to assure their usefulness in leprosy research.*

## 12. MEDLINE/Brazil

The MEDLINE/Brazil system currently operates in seven cities of Brazil from Fortaleza to São Paulo. The software provided by the U.S. National Library of Medicine (NLM) is updated monthly on an IBM 370/155 located at the State of São Paulo's Atomic Energy Institute in São Paulo.

The system was developed with the aid of a grant to Brazil from the United Nations Development Program, and is managed by PAHO's Regional Library of Medicine and the Health Sciences. Utilization level averages 2 hours per week per terminal with a fee of Cr\$ 85.00 per bibliography to defray computer and telecommunications costs.

A Selective Dissemination of Information (SDI) service based on bibliographies obtained from MEDLINE/Brazil is available in the States of Rio Grande do Sul, Rio de Janeiro, and São Paulo and in the city of Belo Horizonte at a yearly cost of Cr\$ 864.00 per user. \$ 28<sup>00</sup>

The expansion of MEDLINE/Brazil is continuing in close cooperation with the Instituto Brasileiro de Informação em Ciência e Tecnologia (IBICT). Terminals in the cities of Belém, Campinas, Curitiba, Florianópolis, Niterói, Pôrto Alegre, Rio de Janeiro, and São Paulo will be added by late July 1976. Additional data bases including CANCERLINE, CANCERPROJ, and an audiovisual listing are planned, as well as collateral uses of the network for biomedical purposes other than bibliographic reference. Development of a regional Latin American biomedical teleprocessing system as an extension of the Brazilian system is under discussion.

*The Committee expressed interest in this project and saw a demonstration through terminals especially installed at the PAHO building in Brasília. The Committee was concerned that much of the information produced in local journals, theses, and other publications was not available. It was also felt that some of the impact of this project might be lost because the journals were not available after the bibliography requested was produced. It was pointed out, however, that the Brazilian Government had a definite policy to enrich local libraries.\* The feeling of the Committee was that MEDLINE was an excellent service which was expanding, improving, and contributing usefully to scientific work in Brazil.*

13. Review of the Activities of the PAHO/WHO Immunology Research and Training Center in São Paulo

The PAHO/WHO Immunology Research and Training Center (IRTC) has two main objectives: to provide candidates from Latin American countries with

*\*Secretary's note: About 88 percent of the photocopy requests received by RLM are satisfied through the resources of that Library, or those of the libraries of its network, as shown in Research in Progress 1976 and other current documentation on the Library.*

postgraduate training in basic immunology, and to give support to research projects directly or indirectly related to health problems in the Region. The first objective is being successfully achieved through 4-month annual courses on basic immunology given by local and visiting professors. The IRTC also offers occasional courses on immunological aspects of local health problems. A course on lymphocyte transformation and macrophage cultivation in leprosy was given in 1974 and a course on immunology of Chagas' disease was due to be held in July 1976. The IRTC accepts as fellows graduate students of the University of São Paulo and the Escola Paulista de Medicina to carry on their research projects. The research activities of IRTC concentrate on problems of immediate hypersensitivity and Chagas' disease.

*The Committee noted that although fellowships were available, relatively few students came from countries other than Brazil. The point was made that training schemes were only useful if the trainees returned home, but that lack of basic facilities at home often militated against this. However, a remarkably high proportion of the students trained had remained in Latin America. The Committee agreed that satisfactory training was being given in immunologic methods but expressed some concern over the nature of the research being done. It was proposed that PAHO should re-examine the mission of the Center in the light of present needs and performance.*

#### 14. Maternal and Child Health Development Program

The overall objective of this 5-year Program is the development of service methodology through operational studies in the priority areas defined by the Inter-American Investigation of Mortality in Childhood already completed, and of human resources for maternal and child health and family health programs, including activities in rural areas wherever feasible. Eight local projects have been or are being planned in Brazil and constitute the Brazilian component.

The Brazilian community health projects with emphasis on maternal and child health are located in: Fortaleza (Ceará); Recife (Pernambuco);

Campos and Niteroi (Rio de Janeiro); Londrina (Paraná); Porto Nacional and Goiânia (Goiás); Belém (Pará); and Santo André (São Paulo). Projects in Fortaleza, Recife, Campos, Porto Nacional, and Belém include both urban and rural areas.

All these projects constitute by themselves large operational studies as well as open schools for training human resources for health at all levels and for conduct of epidemiologic and community-centered research.

*The Committee received this report with great interest. It was impressed with the emphasis being placed on the utilization of local resources and the fact that the program had been grafted onto several agencies already in existence. There was considerable discussion on the method by which food supplementation programs should be introduced and the devices to be used to get any target group to accept the supplement.*

*The Committee was told that in Brazil the introduction of a new form of death certificate and of a new form of birth certificate (containing the item "birthweight") would provide additional information including data on congenital anomalies. The relationship between economic development, movement of peoples, and health development programs was stressed.*

*These action programs, which have been started in Brazil, provide an excellent opportunity for applied research urgently needed for the development of nutrition policy and planning (see item 16). For example, it is known that nutritional intervention during pregnancy in populations with marginal dietary intakes can improve the infant's birthweight and its chances of survival. Information is needed about how early in pregnancy the intervention should be made and what magnitude of intake should be achieved.*

*Furthermore, in any action program aimed at a large number of beneficiaries it is expected that a gradient of intakes will be observed. This allows the possibility of answering many questions concerning the relationship between the amount of duration of supplementation and its effectiveness, i.e., the functional, social, and economic consequences, in the short and long term, of different levels of supplementation. Effects on community organization and functions must also be considered.*

*This question was considered again in the Executive Session (see item 22, page 36).*

15. Program Development at the Center for Human Ecology and Health

The Pan American Center for Human Ecology and Health (ECO) was officially established in Mexico City in September 1975, following the signing of an agreement between the Pan American Health Organization and the Government of Mexico. A meeting of advisors, held earlier, stated that the role of the Center should be "to integrate and analyze existing knowledge, to foster links between sectors within social systems, and to evaluate the consequences of planned and unplanned actions."

The Center for Human Ecology and Health plans, at the request of member governments, to conduct and manage assessments of the impact of social and economic development activities on human health. The assessment activities include analyses of the existing situation, projections as to the ecologic and health consequences of the process or project, and assistance in the formulation and implementation of appropriate environmental control standards and strategies.

At first, emphasis will be on conducting assessments, but as experience is gained, emphasis will shift to supporting the growth of national assessment capacity by transferring and adapting methodologies, training personnel, and providing current information. The nature of the task assigned to the Center dictates a broad ecologic approach to health problems, requires the development of multidisciplinary teams, and implies a systems approach to the description and analysis of complex problems. The emphasis will be on appropriate application of existing knowledge rather than on basic research.

Following a 2-year planning and development phase which started in 1975, the Center expects to grow to its full capacity and productivity within 5 years, leveling off at a staff of 9 professionals and an annual budget of about \$600,000.



The Committee was very interested in this new PAHO center and accepted the view that one of ECO's early tasks should be an educational campaign to acquaint member countries with its existence and potential. It was stressed that study of social structure in general and governmental structure in particular is an essential prerequisite to formulating plans to study the impact of development on health. Countries should be encouraged to build environmental assessment into their development plans at an early stage.

The Committee felt that this field of work was so important that an Advisory Committee for the Center should be established as soon as possible. One of the first functions of this Committee would be to help with the appointment of new staff. In this connection the ACMR proposed that an Advisory Committee should also be appointed for the Pan American Center for Sanitary Engineering and Environmental Sciences (CEPIS) in Lima, Peru.

#### 16. National Food and Nutrition Policy

During the technical discussions of the XXIII Meeting of the Directing Council of the Pan American Health Organization, which took place at Washington, D.C. on 3 October 1975, there was a review of the elements involved in the formulation and implementation of national food and nutrition policies, as well as of the nutrition and food situation in Latin America and the Caribbean.

Because several sectors are involved in nutrition, they must all help to develop a food and nutrition policy and collaborate fully in its implementation. It may be necessary to have a political decision at a very high level to insure that there is intersectorial coordination and collaboration.

It is also proper that the health sector should give priority to strengthening and expanding nutritional activities in primary health services as an integral part of family health programs, as well as to undertaking nutritional surveillance of the high-risk groups. There should also be preventive measures for the control of specific nutritional diseases. Attempts must be made to improve the food situation in institutions by strengthening the technical and administrative services they provide. The health sector should be concerned with nutrition training of all personnel, especially those at intermediate and auxiliary level.

The realization of many of these aims would also be helped by having properly trained planning officers and paying attention to continuing evaluation of all nutrition programs. It was also agreed that attention must be paid to priorities in food and nutrition research and perhaps the following goals were appropriate: to find new sources of food; to increase the nutritive value of existing foods; and to convert agricultural byproducts, now wasted, into animal feeds.

*The Committee discussed this report and its implications. The view was expressed that in laying emphasis on food and nutrition, it must not be forgotten that poverty is probably the major determinant of the low level of nutrition of large sections of the world's population. The Committee was concerned that food and nutrition policies should not ignore the fact that much research was needed to find the best method of implementing these policies and rapid indicators of the effect of these policies.*

*For a nutrition policy to be effective, it has to start with the identification of what kinds of people are malnourished or at different degrees of risk of becoming malnourished. The presently available methods for the assessment of nutritional status are costly and represent a significant portion of the scarce resources available for nutrition improvement activities in most countries. Moreover, the typical survey is time-consuming, its results take a long time to be available, and it only indicates present nutritional status. For adequate nutrition planning, it is necessary to know the trend of change in nutritional status. Therefore, research is urgently needed on the identification of parameters that are highly sensitive to changes in nutritional input and that would indicate nutritional status and changes in nutritional status. Obviously, it is required that these indicators give reliable information for different age-sex groups.*

*It should be clear also that a food policy is separate from a nutrition policy and attention must be given to establishing the nutritional aspect of various food policies. The Committee was anxious to see proper surveillance built into any of these policies. There was much discussion as to the best method of insuring that, within the governmental structure, the health sector received the support it needed to carry out its programs.*

The Committee was eager to see that everything possible was done to carry out the recommendations of the PAHO Directing Council, and a specific proposal was made in the Executive Session (see item 22, page 36).

17. Report of the Scientific Advisory Committee Meeting on Dengue, Yellow Fever, and *Aedes aegypti*

The first meeting of the PAHO Scientific Advisory Committee on Dengue, Yellow Fever, and *Aedes aegypti* was held in the Gorgas Memorial Laboratory, Panama City, Panama, on 22-26 March 1976.

The previous Scientific Advisory Committee on Dengue had recommended in 1974, that it be reconstituted to include experts in yellow fever and *Aedes aegypti*, so as to cover the entire problem of *Aedes aegypti*-borne diseases, their prevention, control, and surveillance. The resolution on this recommendation was adopted by PAHO's XXIII Directing Council Meeting on October 1975.

The continued risk of sylvatic yellow fever was emphasized, as sizable epidemics had been recorded in the past 10 years. The recent outbreaks of dengue fever in Colombia and Puerto Rico emphasize the continuing potential risk of this *Aedes aegypti*-borne disease. There is a risk of dengue hemorrhagic fever in the Americas, with the presence of dengue-2 and dengue-3 in the same country, the growth of urban populations and their crowding, the high rates of *Aedes aegypti* infestation, the increasing human traffic between towns and countries and the observation that hemorrhagic manifestations have occurred in Puerto Rico.

The current status of the *Aedes aegypti* eradication program was reviewed. Seventeen countries or territories are now free of *Aedes aegypti*; 34 are still infested, of which 20 have active campaigns, and 14 are engaged in limited activities or have no eradication program. The important mainland areas which are not participating in the eradication program at the present time, are the United States and parts of Venezuela.

In the discussion of vaccination, the following points were emphasized. Yellow fever vaccine is produced by only three manufacturers in the Americas.

If an emergency situation occurred, a limiting factor would be the small quantity of secondary seed lots at present available. It was recommended that at least 4,000 ampoules be obtained immediately for such emergencies. Research on dengue vaccine is in progress in three laboratories in the United States. However, development of a multivalent vaccine will probably not come for several more years.

For the prevention of yellow fever and dengue, three other possible strategies were considered. The first would be to abandon Aedes aegypti eradication and control programs and maintain surveillance for yellow fever and dengue, instituting yellow fever vaccination and emergency vector control only when necessary. A second possibility would be to abandon the eradication policy and attempt to maintain hemispheric-wide control of Aedes aegypti levels sufficiently low to make disease transmission unlikely. A third possibility would be to adopt a flexible policy which recognizes subregional differences, continuing eradication wherever it has been achieved and extending eradication to new areas wherever possible, utilizing vector control, disease surveillance, and yellow fever vaccination as required on a subregional basis to provide maximal protection of the population against yellow fever and dengue. The third possibility was adopted and a supplemental report was prepared for consideration by the Directing Council of PAHO.

This supplemental report stated that there was total agreement that eradicating Aedes aegypti is the most effective measure to prevent urban yellow fever and dengue. In addition, eradication is technologically possible, provided financial resources are available, and all hemispheric countries agree. However, since resources are limited and costs increasing, some nations may not consider eradication as a justifiable program. Therefore, the adoption of a more flexible policy was recommended. Several specific operational and research recommendations were made relating to disease and vector surveillance, vector control, and vaccination aimed at improving protection against yellow fever and dengue.

*The Committee received this report with interest. The advisability of continuing and intensifying research on genetic manipulation and biological control as a tool in anti-Aedes aegypti campaigns was raised. The Committee*

discussed the preparation of vaccine against dengue and considered the necessity for a policy-decision as to whether a vaccine would be used even if it were developed. The problems of a polyvalent versus monovalent vaccines were discussed, as well as the possibility that the ideal approach to epidemic dengue might be rapid isolation of the strain and widespread vaccination with the type-specific vaccine. It was stressed that many of these epidemics of dengue showed that surveillance had broken down at a management level.

The Committee commended the work of the Scientific Advisory Committee, and considered it important that PAHO should maintain it in operation on a continuing basis.

18. Report on the Scientific Advisory Committee Meeting on Meningococcal Disease

The first regional meeting on cerebrospinal meningitis organized by PAHO in cooperation with the Government of Brazil and the Member States took place in São Paulo and Brasília, Brazil, on 23-28 February 1976. The objectives set forward for the Scientific Advisory Group were: (1) to review the subject of cerebrospinal meningitis in general and the situation in Brazil in particular; (2) to analyze the experience gained in Brazil with regard to laboratory diagnosis, treatment, and factors influencing mortality among hospitalized patients; and (3) to review scientific knowledge and techniques, and on this basis to develop strategies for prevention and control.

The experience during the Brazil epidemic of 1971-1975 emphasized the need for public information and effective surveillance. Every health service should be encouraged to upgrade its laboratory facilities for the diagnosis of Neisseria meningitidis from suspected cases. Reference laboratories should include facilities for isolation, grouping, and testing of meningococci for drug resistance.

There is evidence from Brazil that, during an epidemic, immunization may prevent disease in a major proportion of the expected patient population

and reduce the severity of the disease in the remainder. Because it is not presently possible to predict an epidemic of meningococcal meningitis, routine use of the vaccine, which is currently available, is not recommended at the present time. Early epidemiologic identification of outbreaks, possibly through such indicators as shifts in the age-specific incidence of disease, introduction of new serogroups, and the presence of "virulent" strains would provide the optimal situation for vaccine usage. Environmental methods of control (e.g., isolation and housing sanitation) lack quantitative documentation of their relative effectiveness.

The role of chemoprophylaxis should be reassessed. Although Rifampin and minocycline are effective in eradicating meningococci from the nasopharynx, their widespread use in civilian populations is likely to be ineffective. Treatment of any clinical case should be initiated with intravenous penicillin or ampicillin within an hour after the patient is seen. Steroids and vasopressors are of questionable value.

The Scientific Group identified particular areas for further studies and research:

(1) The stability of both meningococcal polysaccharide vaccines, particularly group A vaccine. Pending development of improved vaccines, attention should be directed to the practical problems of vaccine transportation and storage.

(2) The development of a group B vaccine.

(3) Methods of serogrouping (e.g., precipitation technique) should be improved and popularized. Additional epidemiologic studies are needed to substantiate evidence that the type 2 outer cell wall protein antigen is associated with virulence.

(4) Epidemiologic studies to determine the effectiveness and duration of immunity following revaccination with meningococcal polysaccharide vaccines.

(5) Epidemiologic studies to document the relative effectiveness of housing and sanitary conditions in determining the incidence of the disease.

(6) Promotion of the development of improved chemoprophylactic regimens or agents.

In its final statement the Scientific Group strongly recommended that PAHO establish a regional program for meningitis control, including provision of basic diagnostic facilities, expert advice, dissemination of information, meningococcal surveillance, and assistance in the immediate acquisition of vaccines.

*The Committee discussed this report, and the view was put forward that ultimate control of the disease may not be in the production of a capsular polysaccharide vaccine but in the search for avirulent strains of meningococci. The recommendation that persons of all ages be vaccinated was questioned. The Brazilian experience was that this exercise, though costly, was beneficial. The magnitude of the global problem of meningococcal meningitis was stressed, and it was hoped that workers in the African continent might be involved in the research of the meeting's participants.*

*The Committee supported the Scientific Group's recommendation that PAHO should initiate a regional program for meningitis control.*

19. Report on the Scientific Advisory Committee Meeting on the Caribbean Epidemiology Centre (CAREC)

Guidelines for the Centre's four-point program--surveillance, laboratory services, training, and research--were developed from the results of a survey of local surveillance systems and laboratories carried out in 16 of the participating countries or other political units.

A course in basic surveillance for area epidemiologists was held in May. Between that time and the end of the year, the number of countries or other political units reporting regularly to CAREC rose from 7 to 16, information from 2 of them being received weekly by telephone.

There has been a general improvement in the quality of the data submitted. In accordance with the meeting's recommendations, Jamaica introduced new reporting forms and procedures. Grenada set up an entirely new surveillance system which involves the collection of data by district

nurses from weekly clinics and also the daily reporting of hospital admissions to the newly established surveillance office, to which a trained medical records officer has been assigned. In a number of places study was being given to the possible notification of diseases such as gastroenteritis and malnutrition.

A 3-day workshop on Pan Caribbean surveillance (Port of Spain, December 1975) attracted 35 participants from 28 countries or other political units in Central America and the Caribbean area. Agreement was reached on methods for the exchange of information, and areas for future work were identified. Particular emphasis was placed on the need for quality control in laboratories and close cooperation with animal health services in regard to the zoonoses.

The Centre's epidemiologists visited each territory on a regular, scheduled basis. In addition, CAREC rendered ad hoc advisory services in many instances, and special visits were made to Belize, in connection with a histoplasmosis survey, and to Grenada, to investigate cases of typhoid fever.

In-service training programs in surveillance for health personnel, including physicians, nurses, public health inspectors, and statistical workers, were held in Belize, Grenada, Jamaica, and Trinidad and Tobago.

Studies were conducted at the Centre in association with the Trinidad Public Health Laboratory on respiratory infections, pyrexia of unknown origin, jaundice, and central nervous system disorders. Serology were used in the yellow fever surveillance program and in estimation of the effectiveness of poliomyelitis vaccination in Barbados, and a broad survey of poliomyelitis antibody levels throughout the Caribbean area was initiated. CAREC cooperated with the authorities in Dominica and the U.K. Medical Research Council in a detailed study of the interrelationship of intestinal parasites, hemoglobino-  
pathy, and immune status in 1,000 schoolchildren between the ages of 1 and 10. Research was also conducted on rabies (in Grenada), leptospirosis (in Trinidad and Tobago), blackfly (in Guyana), and on immune response in streptococcal disease.



Publication of a monthly surveillance report began in March 1975. The report carries a digest of communicable disease statistics from the Caribbean, as well as articles on topics of particular significance to the area. Circulation of this report is now 1,000 copies per month and the number of participating territories has risen from 7 to over 20.

*The Committee received this report and congratulated the Centre for the amount of work it had achieved during the consolidation phase. It expressed the concern that the Centre should not expand its program too far beyond the original unit. The work of the Centre on gastroenteritis was noted. Gastroenteritis, being also related to water and sanitation, the Centre should strive to improve bacteriology of water in the region when personnel was available. In general, laboratory facilities at the Centre need to be strengthened. The Committee also noted that same attention should be given to the behavioral sciences and genetics in epidemiology centers since the evidence was now very strong that investigations of human behavior would throw considerable light on the epidemiology of various diseases.*

*It was recommended that PAHO should initiate a program for the investigation of the role of the rotavirus in the gastroenteritis which is so common in the region.*

*The Committee paid particular notice to the work on the blackfly problem in the Rupununi district in Guyana.*

*In view of the growing importance of blackflies as a serious pest problem in development projects of river valleys in tropical America and the possible spread of onchocerciasis as a result of large movements of human populations, the Committee recommended that PAHO stimulate research on the systematics and natural history of blackflies in tropical America.*

20. Report on the Scientific Advisory Committee Meeting  
on the Pan American Foot-and-Mouth Disease Center

The Scientific Advisory Committee to the Pan American Foot-and-Mouth Disease Center (SAC/FMD) met on 10-14 November 1975. The importance of this disease is partly shown by the fact that government investments

to control foot-and-mouth disease (FMD) have reached over \$200 million. Support for this endeavor is also received from the Inter-American Development Bank (IDB).

A regional laboratory is being planned in Panama for diagnosis of vesicular diseases in order to relieve partially the Center in Rio de Janeiro of some responsibilities and to permit the much needed expansion in vesicular disease surveillance.

Since epidemiological patterns of FMD in South America are still not clearly defined, all opportunities to collect additional quantitative data should be utilized.

Disease reporting by South American nations provides essential information for the disease security of all nations. A few countries report on the number of cases of FMD by geographic location each week, others every 2 weeks, and some only every 16 weeks. The current situation is an improvement over that of the past but greater uniformity of reports and increased frequency of reporting is desirable. Ongoing training programs in epidemiology and diagnostic methods should help toward the goal of increased disease reporting and gathering of epizootiologic information in every nation in the Hemisphere.

In consultation with the IDB, a proposal for determining the physical losses from FMD in milk and beef herds on selected farms in the state of Rio de Janeiro was reviewed. Recommendations were made that this study provide information on losses from FMD which can be interpreted into economic terms (see item 10, page 17).

The PAHO-FMD Center has had interest for many years in oil adjuvanted FMD vaccines. The Advisory Committee of the Center had emphasized the importance of field testing this vaccine as soon as possible and recommended that tests be carried out using vaccine manufactured under strict control of the Center including the potency testing by challenge. A 2-year study was projected which should give excellent information on the comparative value of oil-adjuvanted and aluminum hydroxide vaccines.

The Center is developing improved methods to evaluate the serologic relationship of FMD virus strains within a single type, as well as to

determine the degree of cross protection afforded by the individual strains against others within the same immunologic type. In view of the expected benefits, the project should be continued and extended to include information on a bank of sera against all subtypes existing among the three immunologic types of FMD virus in the Hemisphere.

Training activities of the Center have increased tremendously and should be further expanded. The Center was encouraged to work with other institutions of PAHO in affording opportunities for postgraduate study.

*The ACMR, in discussing this report, was enthusiastic in its support for a center which was clearly performing excellent work and carrying out very good training programs. It was felt that the surveillance system should be further developed and extended and the Committee strongly supported close relationship between this institution and other PAHO and government centers.*

*It was also suggested that the Director of the FMD Center should be requested to present a proposal with a budget to PAHO for expanding facilities to develop a live attenuated FMD vaccine. In view of the constricting finances of the Foot-and-Mouth Disease Center and of its great importance to the member countries, the Committee strongly recommends that PAHO strengthen the budget of the Center, so that it may not be forced to curtail any of its present programs.*

21. Report on the Scientific Advisory Committee Meeting on the PAHO Regional Library of Medicine and the Health Sciences

The VIII Meeting of the Scientific Advisory Committee on PAHO's Regional Library of Medicine and the Health Sciences (RLM) was held on 11-13 December 1975 at RLM in São Paulo.

Following a presentation on the status of interlibrary agreements between RLM and biomedical or central libraries in Brazil and other countries, which define the PAHO library network, there was a report on RLM's current budget (1975) and proposed budget for 1976. It was noted that the 3-year projects financed by the Commonwealth Fund (general library support)

and the W. K. Kellogg Foundation (training of biomedical librarians) were terminated at the end of 1975.

A grant application to the Brazilian agency Financiadora de Estudos e Projetos (FINEP) totalling Cr\$ 17,207,000.00 for 3 years, was approved in June 1976. Its main purpose is to provide technical assistance and equipment to libraries of Brazil's biomedical library network.

The Committee was also briefed on the status of RLM's Audiovisual Center, which is being developed under the same grant from the United Nations Development Program (UNDP) to PAHO as that for the MEDLINE system in Brazil (see item 12, page 19). A related program of Selective Dissemination of Information (SDI) developed by RLM with bibliographies generated by MEDLINE was also described. This "current awareness" program serves rural areas and thus both complements the MEDLINE/Brazil system and serves as a precursor service. Another significant development was the completion of nationwide union catalogs of periodicals by several Latin American countries.

*The Committee urged that, in allocating limited resources and in view of the rapidly increasing costs of scientific periodicals and books, a balance be kept between assuring continuing availability of new reference material, and the mechanics of its dissemination.*

*The Committee endorsed the recommendation of RLM's Advisory Committee that a well-known distinguished medical scientist with a biomedical research and training background, should be appointed Director as soon as possible.*

*In its concluding recommendation, the Committee urged the strengthening of RLM's administration and management, expansion of MEDLINE services to other Brazilian cities and Latin American countries, a systematic approach to periodicals acquisition, continuation of the RLM training program and promotion of SDI services.*

*The ACMR was interested in these other aspects of the scientific information services in Brazil. It was suggested that PAHO, through its Regional Library, might help pharmaceutical practice not only by circulating*

*the Medical Letter, but also by providing information as medical inserts for packages of drugs. Such information is mandatory in the United States.*

## 22. Executive Session

### 1. Statement of the Director

Dr. Acuña outlined his views on the composition and function of the ACMR. He recognized that the ACMR should play a more active role in the formulation of research policy, and for this reason stressed the importance of continuity of the Office of Chairman. The Chairman would have direct contact with the governing bodies of PAHO, report to the Directing Council on the activities of the ACMR and in turn report back to the ACMR on the needs for specific research as identified by the Health Ministries of the Region. He pointed out that PAHO's research interests must be consonant with the expressed priority areas in health. These are:

(a) Strengthening of the health services and extending coverage to rural and underserved areas.

(b) Control of disease, especially communicable diseases. Although vertical campaigns against specific diseases have been successful so far, an infrastructure of health services is needed for every country.

(c) Development of human resources and research activities to support the requirements of the above infrastructure. In the network of health services, professionals, technicians, and ancillary personnel-- including voluntary workers at the community level--need to be trained.

(d) Family health and family planning, with emphasis on mothers and children.

(e) Environmental health. Activities must deal with water supply, sewage disposal, and the growing problem caused by urbanization and industrialization, i.e., solid waste and environmental pollution.

PAHO is concerned that attention should be given to the development of an indigenous technology that is relevant to local cultural, social, and economic conditions. Dr. Acuña felt that the major aim of the ACMR was to identify problems and find solutions within the sociocultural environment of the area.

To fulfill this role he suggested that the ACMR might have subcommittees which would play a part in insuring that the PAHO research and training institutions in the area discharge their specific functions more effectively. He also suggested that members of the ACMR might participate in the work of the technical advisory committees which have been established in most of the PAHO institutes and centers, but which are not all functioning very well. This would be one mechanism for establishing close relationship between the ACMR and the actual research program.

Finally, Dr. Acuña explained that although he was responsible for appointing the members of the ACMR, he wished the Committee to elect its own Chairman and Vice Chairman. He suggested that the functions of the Committee, as he envisaged them in the immediate future, would best be carried out for the next term under the Chairmanship of someone from the Latin American region. He also urged members to consider such things as the duration of tenure of the Chairman, the length of service of members, and the possible need for new members.

In response to questions, Dr. Acuña pointed out that finance would probably not be a major constraint in reorganizing the work of the Committee. If the ACMR makes proposals that cannot be covered from existing resources, they will have to be submitted to the PAHO Governing Bodies.

The Director also reported that WHO is now establishing regional ACMRs, and that funds for research might become available to PAHO from WHO. Moreover, to the extent that research is related to the needs and health programs of countries, it should not be too difficult to fund it.

The Director then withdrew.

## 2. Objectives

The Chairman pointed out that on many occasions in the past the ACMR had expressed the wish to be more closely involved in planning and in advising on research objectives, policies, and strategies. The Committee therefore welcomed the clear statement by the Director of PAHO that he wished the ACMR to undertake these new responsibilities.

## 3. Methods of operation

The Committee accepted that it was not possible in the present session to plan in any detail the ways in which they should tackle these new responsibilities. After discussion, certain principles were however agreed:

(a) The ACMR should regard itself as operating continuously throughout the year, and not simply at its annual meetings.

(b) Research strategies must be developed in relation to the priority areas designated by the Director. To be realistic, they must also take account of the internal organization of PAHO, according to which each division has responsibilities for two or three centers.

(c) Priorities cannot be established and gaps identified until there has been time for analysis of the available information about what is being done. However, there are some obvious priority areas, e.g., health services research, in which the ACMR does not at present have the expertise to make a proper review. Such deficiencies will have to be made good (see below).

(d) In view of the high priority given by the Director of PAHO to expanding and strengthening the coverage of health services, community-centered research projects are highly advisable, and during the coming year members of the Committee should explore possibilities of such research in Latin America. It is hoped that a subcommittee for recommendations in this high-priority field will serve in the future.

(e) It will obviously not be possible to review all subject areas within 1 year. In the meantime, a start might be made in three areas that are likely to have priority in any overall strategy: communicable diseases,

nutrition, and human ecology. Individual members of the ACMR accepted the responsibility of initiating new policy reviews in these three fields.

*Nutrition - Dr. Cravioto*

*Communicable diseases - Dr. Galindo*

*Human ecology - Dr. Monge*

They would organize subcommittees or working groups and would be assisted as required by other members of the Committee. It was hoped that at least a preliminary policy document in each of these fields would be presented to the Committee next year.

(f) The Committee accepted the suggestion that they should be more closely associated with the research planning of PAHO centers, and with reviewing their achievements. This could be done by associating individual ACMR members to the technical advisory committees of these centers, or by any other appropriate mechanism.

#### 4. Other initiatives

(a) Dr. Chagas offered to prepare two papers for discussion by the Committee next year: (i) A paper on the equilibrium between the transfer of technology and the building up of indigenous scientific manpower; and (ii) A report of a scientific meeting to be held in October on the use of natural products in the protection of agricultural plants.

(b) The ACMR recommended to PAHO the appointment of a subcommittee (i) to advise on research in the linked fields of nutrition policy and planning, and maternal and child health (see items 14 and 16, pages 21 and 24); (ii) to consider specifically the possibility of establishing a demonstration area on food and nutrition policy; and (iii) to examine and utilize indicators for rapid assessment of changes in nutritional state of population, and consider operational research which might be dovetailed on food supplementation programs.



5. Membership of the Committee

(a) It was recommended that members should be appointed for up to 4 years, with at least 1-year interval before reappointment and with designation for annual replacements.

(b) It was recommended that new members should be appointed to cover the disciplines of health services research, social sciences, immunology, occupational health, and veterinary medicine. The Committee does not attach priority ratings to any of these except health services research.

Since some members are retiring this would not necessarily mean any substantial enlargement of the Committee.

Members are encouraged to send to the Director names of suitable individuals in these disciplines.

6. Chairman and Vice-Chairman

(a) It was unanimously agreed to recommend to the Director that Dr. Carlos Chagas should be appointed Chairman and Dr. Joaquín Cravioto Vice-Chairman.

(b) It was agreed that the Chairman should hold office for 2 years, and that the Vice Chairman should automatically succeed him. Thus a new Vice-Chairman would have to be elected every 2 years.

(c) It was agreed that the Vice-Chairman is not merely a deputy for the Chairman but has responsibility for an active part in the continuing work of the Committee throughout the year.

7. Acknowledgments

At the conclusion of the Executive Session the Committee wished to put on record its appreciation of the excellent service given to it by the Secretary, Dr. M. Martins da Silva. The wide range of topics discussed at this and previous meetings reflects the extent of his contribution to PAHO's research program, for the development of which he has been

responsible over the last 15 years. The high standing of PAHO's record in research is largely due to his energy, his wide contacts in the scientific community and his insight into the needs of the region.

The Committee, in turn, thanked the departing Chairman for the service he had given and the way in which he had handled the meetings over the past 5 years.

23. Plans for next year's meeting

This question was not discussed for lack of time. The ACMR requested the Chairman and Vice-Chairman, in consultation with the ACMR Secretary, to consider the structure and agenda of the next meeting in the light of the ACMR's new responsibilities.

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