PAN AMERICAN HEALTH ORGANIZATION

ADVISORY COMMITTEE ON MEDICAL RESEARCH

THIRTEENTH MEETING

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WASHINGTON, D.C.

REPORT TO THE DIRECTOR

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Advisory Committee on Medical Research
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PAHO ADVISORY COMMITTEE ON MEDICAL RESEARCH

Report to the Director

1974

Introduction

The Thirteenth Meeting of the PAHO Advisory Committee on Medical Research was opened by the Chairman, Professor John C. Waterlow, who called on the Director, Dr. Abraham Horwitz, to deliver his address.

Dr. Horwitz started by extending greetings to two new members of the Committee: Dr. Pablo Purriel from Uruguay and Dr. G. Malcolm Brown from Canada. He regretted the absence of Drs. Aujaleu, McDermott, and Sabin, and recorded with deep sorrow the death of Dr. Herman Hilleboe, for several years a devoted member of this Committee. Dr. Hilleboe had made many contributions on health planning and public health administration, and had chaired the Symposium on Systems Analysis Applied to Health Services that was held during the Tenth Meeting of the Advisory Committee on Medical Research. The Director expressed his appreciation to Dean Myron Wegman and to Professors Abel Wolman and John Hanlon for organizing the respective symposia on the role of schools of public health in the development of health care in the Americas and ecology and pollution in the Americas. Dr. Horwitz concluded his address with a short review of the topics to be covered during the 5-day meeting.

1. Control of disease in Amerindians in cultural transition

PAHO has been supporting investigations on the health status of people in isolated or semiisolated Indian villages in Venezuela and Brazil. The information presented was based on studies of Xavante, Cayapó, Yanomama, and Makiritare of the Orinocco and Amazon drainage basins as representatives of tribes in rapid transition, and of the Macushi, Wapishana, Krao, and Piarôa as tribes well advanced in the process of cultural contact.

Uncontacted primitive Indians in general enjoy robust health. A key factor in this has been child spacing, accomplished by a variety of measures including at last resort, infanticide. The average interval in which a Yanomama woman introduces a new child into the culture is about 3 1/2 to 4 years. In the past, health deterioration has mainly resulted from the introduction of epidemic diseases and alcohol. Given the immunization programs, the antibiotics now available, and the improvement of measures to prevent the introduction of alcohol, these factors need no longer be a major problem.

Much discussion was concentrated on the susceptibility of the Indian to epidemic and venereal diseases: smallpox, measles, pertussis, tuberculosis, syphilis, and gonorrhea. The results presented provide no support for the old theory of increased susceptibility of these populations, unless malnutrition is present as well. It was emphasized that gamma globulin levels among the Indians are roughly twice those found in people living in the cities, reflecting the antibody response to continuous endemic diseases.

In a measles epidemic, the production of antibody and the activity of mixed lymphocyte cultures were found to be similar to those of people in the United States. The high mortality resulted from the complete absence of any care for the sick, since almost everyone in the community was affected.

Abandonment of the nomadic way of life to concentrate the Indians around government or mission posts will lead to an increase

in parasite loads and diarrheal infections, and to the exhaustion of the foods from game and local gardens. It was suggested that the process of acculturation among these Indians should begin to place greater emphasis on introducing supplementary food sources and measures to dispose of human waste, and should not disturb those native customs which have limited population growth and have maintained the balance between population and environmental resources.

In short, the problem is now more a social than a medical one.

The Committee strongly supported the continuation of this work, both for reasons of humanity and because of the scientific results which have been achieved.

2. The mycoses as a potential public health problem in the Trans-Amazon Highway region

The vast area of Amazonia covers almost 5 million square kilometers and has a population of about 7 million people. A system of interlocking highways is being built to open up the region for colonization and exploitation.

The potential health hazards to the population moving into the area are being monitored through a collaborative research program of PAHO, the Walter Reed Army Institute of Research, and the Evandro Chagas Institute in Belém, but so far no attention has been paid to the problem of mycotic infections.

Visits were therefore paid by PAHO consultants to the medical and public health institutions in Belém, Santarém, and Altamira. Discussions with responsible individuals and a review of the available literature revealed that the Amazon area has a wide variety of mycoses. These include skin diseases caused by dermatophytes, subcutaneous mycoses such as chromoblastomycoses, lobomycosis, and sporotrichosis and the systemic diseases of candidiasis, histoplasmosis, and paracoccidioidomycosis. Data on the systemic mycoses are based

on case records, skin tests and serologic surveys, and on isolation of Histoplasma capsulatum from wild rodents and an opossum.

This evidence suggests that the colonists are entering an area with a high potential for mycotic infections. Facilities and trained personnel for the diagnosis of the mycoses are virtually nonexistent. None of the hospitals visited in Altamira and Santarém carried out any cultural diagnostic work. Diagnosis of infectious diseases is not based on isolation and identification of the etiologic agent. Serologic diagnostic techniques are only employed for suspected venereal diseases.

The Committee was very much concerned at the possible spread of mycoses among the new inhabitants of Amazonia and at the lack of proper medical care for prevention and treatment. They were in agreement with the recommendation made by the consultants that a diagnostic reference center be organized that could diagnose mycotic diseases by the isolation and identification of etiologic agents. Hospital laboratory facilities along the Trans-Amazon Highway should also be available for physicians, and technicians should be trained in the procedures used for diagnosis of mycoses.

Finally, a surveillance program should be developed to study the incidence and prevalence of mycotic diseases and to carry out appropriate ecologic and epidemiologic studies of the mycoses with the ultimate aim of controlling them.

The Committee expressed the hope that other centers in Brazil, and in neighboring countries bordering the Amazon region, would participate in this work.

3. Sporozoite-induced immunity in mammalian malaria

A report was presented reviewing progress in immunization against malaria by sporozoites. Criteria for testing antigenicity were described. Only sporozoites collected from the thoracic region (hemocele and salivary glands) induce significant antibody formation and are consistently

infective. Maturation of the antigenic capacity appears to occur in the salivary glands. Corynebacterium parvum, a potent RES stimulant, was shown to increase considerably the nonspecific resistance to sporozoite-induced infections. Administration of this RES stimulant combined with the injection of a single dose of X-irradiated sporozoites, greatly increased the percentage of animals protected against infection. It was observed that antisporozoite antibodies to simian and human malaria are strictly species specific; there were no cross-reactions even between malarial species believed to be closely related. A limited number of experiments in human volunteers have shown that they develop resistance to repeated sporozoite challenge when they were previously immunized by the bite of mosquitoes infected with X-irradiated Plasmodium falciparum.

Much interest was expressed in the mode of action of the adjuvant used to strengthen the immunologic response to sporozoite injection; there is no evidence that sporozoite and Corynebacterium parvum share the same antigen. Another problem of great interest, which was briefly discussed in the report, is the mechanism by which antigenicity develops in sporozoites from the thoracic region, which is lacking in those from the other parts of the mosquito.

The Committee was much impressed by the work that has been done on this subject and recommended the continuation of this promising study.

4. Progress report from the Chagas' Disease Research Unit in Salvador, Brazil

The Chagas' Disease Research Unit has been, for the last 3 years, conducting an investigation into the natural history of Trypanosoma cruzi transmission in a rural area in eastern Brazil (Bahia) where Chagas' disease is endemic. This work, which is being done by a group from the London School of Hygiene and Tropical Medicine, supplements clinical and epidemiologic studies being carried out by Brazilian workers under the direction of Professor A. Prata.

Panstrongylus megistus is the sole domiciliated vector of T. cruzi in the area and has not been found away from domestic premises. Other triatomine bugs occur in sylvatic habitats; Psammolestes tertius in bird nests, Rhodnius domesticus and Triatoma tibiamaculata in epiphytic bromeliads. The latter two species are naturally infected with trypanosomes considered to be T. cruzi, but the vertebrate hosts from which infection is derived are not yet known.

Bugs caught from houses were individually dissected and the rectal contents examined for trypanosomes by phase contrast microscopy. Blood meal squashes of stomach contents were later studied by precipitin tests. Infection rates of household bug populations were discussed in relation to sex and instar and the source of the last blood meal. Man and chickens are the main source of food; chickens, however, are insusceptible to infection with T. cruzi.

The demolition of bug-infested houses, when abandoned by the owners, yielded valuable data on the focalization of bugs within houses, and showed that physically separate subpopulations can occur. The rapid colonization of newly built houses indicates that bugs were introduced passively from the old house with the family goods.

Cats, dogs, and house mice were found to be infected with T. cruzi, as were opossums (Didelphis azarae) and Rattus r. frugivorous trapped near houses. Other animals examined were uninfected. The infection of cats and mice is not considered to have any epidemiologic importance.

In the light of the results obtained so far, possible transmission cycles are discussed and the feeding habits of P. megistus in the investigation area are compared with those found by other workers in their study of the same species elsewhere in Brazil. The eggs of domiciliated P. megistus in the study area are commonly parasitized by Telenomus fariai, a tiny parasitoid wasp.

The Committee recognized the usefulness of this study for understanding the natural history and epidemiology of Chagas' disease; this kind of approach could be extended to other areas where Chagas' disease

is endemic. The Committee agreed that a strong recommendation should be made for continuing further financial support for this work.

5. Mycobacterium ulcerans in the armadillo

Large necrotizing skin ulcers caused by Mycobacterium ulcerans were first described in Australia in 1948. Since then the condition has been found in Bolivia, Mexico, Zaire, Uganda, Nigeria, Ghana, Malaya, New Guinea, and possibly Peru. In spite of the increased recognition of the disease, even in endemic areas where clinicians are aware of it, it is likely that diagnosed cases represent only the "tip of the iceberg". This is probably true in Central and South America, where many chronic ulcers go undiagnosed for months or years. Furthermore, the disease mimics a number of other conditions prevalent in Central and South America and in the past, infection with M. ulcerans has been confused with cutaneous leishmaniasis, tropical phagedenic ulcers, and the cutaneous mycoses.

M. ulcerans infection has a high prevalence in some endemic areas, but there is no evidence that any race, age, or sex is protected or predisposed. In Uganda where M. ulcerans is a major public health hazard, a refugee settlement provided an opportunity for detailed epidemiologic studies. Despite these investigations, the natural reservoir for the organism, the route and method of its entry into man, and the mechanism by which it produces such extensive necrosis remain unknown. M. ulcerans has not been recovered from any natural source (excepting human infection) and epidemiologic studies show clearly that contagion is not an important factor. The organism may be introduced by a specific but minor percutaneous trauma--possibly an insect bite.

Various therapeutic techniques have been tried out but none is completely satisfactory. At present a combination of meticulous and repeated surgical debridement and grafting, systemic rifampicin therapy, and continuous warming of the involved area, seems best. Nevertheless, many weeks of hospital care are required, thus blocking hospital beds.

Experimental infections with M. ulcerans in mice and guinea pigs did not mimic the clinical and histopathologic infections in man. Armadillos inoculated intradermally with a suspension of M. ulcerans developed, however, ulcers at the site in 9 weeks that were characteristic of the lesions seen in the human infection.

M. ulcerans produces a toxin that causes an extensive necrosis with very little inflammatory reaction. Although the chemical composition of the toxin has not yet been fully identified, preliminary studies indicate that it is a protein. An interesting finding is that growth of this microorganism is optimal at 33°C; the body temperature of the armadillo is 33-35°C, and one of the therapeutic measures is continuous warming of the affected area.

The distribution of the infection, which appears to be particularly common in poorly drained and swampy lowlands, poses interesting problems about the epidemiology and the natural reservoir.

The Committee expressed its interest in this work and supported the continuation of the study.

6. Dental caries in Colombian communities

An investigation is being undertaken of the causes underlying an unusually low incidence of dental caries among the inhabitants of the village of Heliconia, a semiisolated community in the mountains to the west of the city of Medellín, in the province of Antioquia, Colombia. The ubiquity of dental caries in most modern urban communities has long been attributed to the consumption of diets rich in fermentable carbohydrate--in particular sucrose. There is, however, solid evidence to show that the deleterious effect is produced by mouth organisms fermenting dietary sugar to acids which, under particular conditions, are capable of initiating the breakdown of tooth enamel.

The unique feature about Heliconia is that the apparent resistance to caries occurs in a population whose diet is particularly rich in sugar.

A staple component of this diet is panela, prepared by heating crushed sugar cane until it crystallizes into a solid brick of sucrose. This is consumed not only at mealtimes but also in drinks and between meals.

Scientists from the University of Antioquia, who were the first to identify the discrepancy between Heliconia and other villages in respect of dental caries, found that children in Heliconia had on average only one third as many carious teeth as their counterparts in other villages. No differences could be found in food consumption and food habits between Heliconia and four other towns. Analyses of the water showed a content of less than 0.2 ppm of fluorine, which is less than one-fifth of what is generally regarded as the optimum level. The water in Heliconia had a high content of magnesium, calcium, molybdenum and vanadium, but the water in the neighboring village of Don Matias, where caries is exceedingly common, had a higher content of manganese, iron, and copper. No indications have been found to suggest genetic differences between populations with different incidence of caries.

A collaborative study into the oral microflora was undertaken by the University of Antioquia, the Pan American Health Organization, and the Royal College of Surgeons of England, beginning in mid-1972. A total of 200 children in Heliconia (low caries) and 200 in Don Matias (high caries) were selected for dental examination. Samples of dental plaque and of saliva were obtained from each child for bacteriologic and chemical studies.

Several possibilities have emerged from the first part of the study, but no single factor has been revealed that would account for the superior dental health of children in Heliconia. Streptococcus mutans, generally accepted as the organism principally concerned in cariogenesis, is substantially more abundant in the mouths of children from the high-caries community (Don Matias) than in the mouths of those from the low-caries area (Heliconia). Dental plaque is present in larger amount and is more cohesive in children from Don Matias than in those from Heliconia. Minor differences have also been detected between samples of saliva taken from the two groups.

Distinctive features have been observed in the physical nature of polysaccharide formed by Streptococcus mutans when grown on sucrose-containing media made up with water from Heliconia, Don Matias, and London. This suggests that elements are present in Heliconia water which influence the formation of polysaccharide from sucrose by the streptococcus.

Discussion was directed particularly towards the composition and properties of Heliconia water. Extremely detailed and elaborate analytical procedures may be required to elucidate chemical differences between different water supplies. In studies of the effects of hard and soft water on cardiovascular disease it has become necessary to go far beyond the limits of conventional water analysis. The fact that a disused salt mine exists in the vicinity of Heliconia, and that the salt from it has a high iodine content, was considered worthy of additional study; mention was made of the fact that the antigoitrous properties of the salt had been recognized more than 100 years ago.

Although the fluoride content of Heliconia water is low, it was reiterated that fluoridation of domestic water remained the one single public health measure proved capable of reducing the incidence of dental caries. Its efficacy is so well established that for the foreseeable future new measures for caries prevention should be regarded as adjuncts.

The ACMR expressed great interest in this work, which is concerned with an extremely important public health problem. The development of this research is an encouraging example of the way in which PAHO has been able to catalyze and stimulate collaboration between outside and local groups. The Committee strongly supported continuing assistance for these studies.

7. Manganese poisoning: a metabolic disease of the brain

Manganese is a potent neurotoxin in industrial workers, and may become an environmental pollutant if it is to replace lead in gasoline.

Therefore, the studies performed in Chilean miners during the last 10 years might become relevant to the general population. In these workers manganese has induced psychosis and later nonprogressive extrapyramidal damage in the central nervous system. Parallel studies on Parkinson's disease have shown that in both disorders the injury to the central nervous system consists in a diminution of synthesis of the neurotransmitter dopamine, which can be restored by overloading the central nervous system with the precursor amino acid, L-dopa. L-dopa treatment of manganese poisoning in Chilean miners has proved successful over a 6-year observation period. In both diseases, L-dopa has produced a sustained correction of extrapyramidal symptoms and signs and a partial correction of the diminution of REM sleep. There are, however, differences in the two disorders, which consist in the absence of L-dopa induced dyskinesia and mental aberrations in patients with manganese poisoning. These side effects, which are observed in patients with Parkinson's disease, are dose dependent and reversible. It appears, therefore, that patients with manganese poisoning have an enhanced tolerance to L-dopa. Furthermore, in the latter patients, high-protein intake does not impair the action of L-dopa, though it has a marked effect in unstable Parkinson's disease patients.

Animal experiments have shown a relationship between manganese intake and concentrations of the catecholamines, dopamine and norepinephrine, in the brains of newborn rats and of their mothers.

Susceptibility to manganese poisoning has been linked to excessive absorption of the metal in patients with iron deficiency anemia and it has been postulated that a potential susceptible group might be newborns and infants. In newborn rats, both the intestinal and the blood brain barrier are not fully developed. If lead is to be replaced in gasoline by manganese, this metal will become a new environmental pollutant, and toxicologic studies have, therefore, to consider newborns and infants as potentially susceptible groups.

The Committee expressed great interest in this work and discussion covered many details of the manganese metabolism and the manifestations

of toxicity. Concern was expressed over the fact that the estimated quantity of manganese likely to be incorporated in gasoline is of the order of one gram per gallon, whereas the concentration in human plasma does not normally exceed 1-2 ng/ml. The amount of manganese likely to be volatilized into the atmosphere has yet to be determined. Although the degree of atmospheric pollution would not remotely approach the concentration obtaining in mines and foundries, the population as a whole, especially children, would be exposed and the duration of exposure would exceed by far that producing effects in miners and foundry workers. Against these fears, however, it has to be remembered that great advantages will be gained from the elimination of lead from gasoline. More information is therefore required about the degree to which contamination of the atmosphere with manganese would occur, and the extent to which manganese would be absorbed, before a firm recommendation is made on the acceptability of adding manganese to gasoline as a commercial practice. The Committee agreed, however, that the situation should be kept under close observation.

8. Brazilian areas of unusually high radioactivity

Three geological areas in Brazil have unusually high levels of exposure to natural radioactivity. These are: (1) the monazite beaches of Guarapari, a city of 20,000 inhabitants in the State of Espírito Santo; (2) the Morro do Ferro, near Poços de Caldas in Minas Gerais; (3) the vicinity of Araxá, also in the State of Minas Gerais.

Studies have been undertaken of the external radiation levels to which the human populations, as well as the flora and fauna, are exposed. The uptake of various radioactive nuclides of the heavy elements in foods and other biota has also been documented.

In Guarapari the inhabitants are exposed to external radiation levels that average about 640 mrem/yr, which is about 6 times the normal exposure at sea level. Studies of food and water contamination in the Guarapari area have indicated, however, that the radioactive materials are tightly bound in the soil and are not ingested in significant amounts.

In another area, near Araxá, the external radiation levels are only moderately elevated, but there is a significant uptake of radium by local crops because of the presence in the soil of a uraniferous phosphate mineral. A dietary survey of a representative sample of the population showed, however, that only 13 percent of 1,500 local inhabitants ingested more than 5 times the normal amount of radium.

The third area of interest is Morro do Ferro, a hill 300 meters high near the city of Poços de Caldas. It is perhaps the most unusual of the world's radioactive areas. Its radioactive part covers a surface of about 0.35 km^2. Gamma radiation levels are as high as 3 mrem/hr. Studies on burrowing mammals have shown that the dose of radioactivity received by the bronchial epithelium of indigenous rats is as high as 3,000 rem/yr.

A study of somatic chromosomal aberrations in peripheral leukocytes has been undertaken in subjects from two of these areas.

In people working directly with the radioactive materials in mills that separate the elements composing the mineral monazite found on the beach of Guarapari, the proportion of cells with deletions and other chromosome aberrations was about 4 times that of controls.

The Brazilian investigations will serve as a model for similar studies that will be conducted throughout the world. Collaborative studies in areas in which humans are exposed to abnormally high levels of ionizing radiation can ultimately contribute in a major way to our understanding of the biologic effects of low-level radiation.

The Committee agreed that these observations were of importance and recommended that investigations be extended. In particular it was felt that the natural phenomenon afforded an opportunity for studying the capacity of DNA to repair following exposure to damaging radiation. There was discussion of animal studies that might be undertaken to determine genetic effects. The Committee took, however, the view that a situation in which the ionizing radiation exposure reached a sixfold increase over the normal, provided a unique opportunity for prospective

human studies and that it was in this direction that effort should be concentrated. The difficulties of such studies should not be underestimated. Very large populations are needed for statistically valid effects to be observed.

9. Considerations on the protection of human beings as subjects of research

Throughout history there has been recognition that a certain amount of human experimentation is necessary, if the benefits of medical research are to be safely passed on to the population in general. At the same time the subjects of such research must not be abused.

Principles to be observed in permissible medical experiments were first enunciated in the Medical Trials at Nuremberg in 1945. These principles constitute what has come to be known as the "Nuremberg Code". They state, in brief, that

- -the voluntary consent of the subject or his representative is absolutely essential;
- -the experiment should be based on the results of prior animal experimentation and a knowledge of the natural history of the problem, so as to insure that the results will be fruitful;
- -the experiment should avoid all unnecessary risk and suffering.

In the early 1960's several governments came to the conclusion that static codes and medical practice laws could not be relied upon as the sole guarantor of the ethics of research projects. It has been generally agreed that a decision to depart from standard and accepted medical practice in a systematic program of clinical investigation requires the approval of the investigator's peers and associates.

In the United States the Public Health Service has, since 1937, employed a peer review system in its reviews of applications for grant

support of research by the nation's universities and laboratories. In 1965, after several demonstrations of poor judgment on the part of investigators, the peer review system was extended into the institutions themselves.

At the moment more than 650 institutions in the United States have established internal review committees to go over research actively in progress within their walls. Such committees to review projects are required to ascertain that:

- -adequate personnel and facilities are available to deal with any probable emergencies during the experiment;
- -the balance between risks and benefits, both to the subject and to the population at large, justify the research; and that
- -adequate, appropriate, and legally effective informed consent will be obtained. The rigor of such consent must reflect the magnitude of the risks to be accepted by the subject.

Health improvements will continue to depend in large measure upon medical research. People's confidence in research is, however, contingent to a large degree on their appreciation of the careful scientific scrutiny of this research, and professional self-discipline in its conduct. As noted by the British Medical Research Council in its 1962-1963 report, "Mistaken or misunderstood investigations could do incalculable harm to medical progress. It is our collective duty... to see that this does not happen...."

In the discussion on this report the Committee gave particular attention to the concept of informed consent, and although it was recognized that the criteria for defining informed consent varied widely in different countries and different cultures, it was generally agreed that there could be no circumstances in which the need for at least an element of informed consent, however assessed, could be dismissed. Upon this, and upon an assessment of the balance between risk and benefit, ethical considerations must inevitably be based.

The Committee recognized that the problems arising from investigations on human subjects were complex in the extreme, and that much thought had been devoted by many national organizations to establishing acceptable codes of conduct.

In addition to these codes, and to the guidance provided by peer committees, a further safeguard is the stand taken by many scientific journals in refusing to publish work which does not conform, in the editor's opinion, to ethical standards.

PAHO has laid down guidelines and has established a review committee at Headquarters, with local committees in each PAHO institute and in each region. All projects supported by or through PAHO will have to be approved by these committees.

The ACMR considered that the subject of the protection of human rights in medical investigations is so important that it must be kept under review. It therefore decided that at next year's meeting it would examine in detail the PAHO guidelines, and the review system which has been set up.

10. The WHO expanded research program in human reproduction

The Expanded Program of Research, Development, and Research Training in Human Reproduction, grew out of WHO's coordination of research efforts in that field. In June 1970, WHO convened a meeting of agencies concerned with promoting research in human reproduction. National medical research councils, technical assistance agencies, and private foundations were among the agencies represented. The exchange of information and views between the various representatives proved to be fruitful, but the picture that emerged of the state of research in the field of human reproduction was not heartening. The meeting noted that existing knowledge of reproductive processes was inadequate and called for a greatly intensified research effort at the fundamental, clinical, pharmacologic, and epidemiologic levels. The meeting also noted that support to

scientists in that field and provision of facilities and equipment were insufficient. One of the recommendations called for a feasibility study to establish a strategy for the further development of research in human reproduction, particularly in fertility regulation, and to define the role that WHO might play in an expanded research effort.

The feasibility study involved consultations with scientists and research administrators and visits to more than 70 research institutions in 25 countries. Its completion in less than a year was made possible by the generous support received both within and outside WHO.

The feasibility study led to the development of a research strategy that is the basis of the WHO Expanded Program of Research, Development, and Research Training in Human Reproduction. The strategy includes defining the objectives of the program; identifying research priorities; creating several interrelated mechanisms for research promotion (namely task forces, research and training centers, and a network of clinical research centers); improving the dissemination of information; and expanding such activities as the provision of research grants, assistance for the publication of proceedings, training awards, consultants, equipment and reagents.

Four major multidisciplinary centers have been designated as Research and Training Centers (two in Europe, one in India, and one in Argentina), and 27 institutes are receiving support as clinical research centers.

A scientific advisory group will meet 2 or 3 times a year to review and make recommendations on research priorities, research strategy, and the allocation of resources. A procedure has been formulated for the scientific assessment of research projects and the long-term evaluation of the program as a whole.

As an example of the type of program which is being supported, research was described into methods for determining the time of

ovulation. The objective of the work is to develop a reference method for ovulation detection in the human female by determining the time interval between the luteinizing hormone (LH) peak and the follicle rupture, and also, the temporal relationship between the first rise and peak of 17 β-estradiol, the first rise of progesterone, the first rise of 17 α-hydroxyprogesterone, and peak of the follicle stimulating hormone (FSH). Ovulation is certified by biopsy of the corpus luteum and/or egg recovery.

With this purpose, the time interval between the LH peak and ovulation in 18 normal cycling women subjected to laparatomy for reasons different than the purpose of the study, were studied. The patients were operated between 2 hours and 144 hours after the LH peak. The timing of the operation was established by the cervical mucus score. Ovulation was certified by either recovery of the egg or corpus luteum biopsy. Plasma LH, 17 β-estradiol, 17 α-hydroxyprogesterone and progesterone were determined by radiommunoassay techniques every 8 hours between days 11 to 15 of the menstrual cycle. Ovulation was certified in 11 patients. In 4 cases the egg was recovered by flushing of the Fallopian tube and in 10 a corpus luteum, aged between 1 to 6 days, was detected. Ovulation was not detected in the patients operated up to 14 hours after the LH peak and certified ovulation was 16 hours. In all the studied patients an estradiol peak preceding LH was found with a minimum interval of 16 hours and a maximum of 48 hours. The initial rise of 17 α-hydroxyprogesterone always preceded the LH rise by at least a minimum time interval of 8 hours. On the contrary the progesterone increment occurred either before, at the same time, or after the LH rise showing no definite pattern. The evidence so far seems to indicate that the time interval between LH peak and ovulation in the human female is a biological constant, as it occurs in other species (rat, rabbit), and that this interval is approximately 24 hours.

The ACMR took note of the WHO Expanded Program, and recognized that projects of the kind described can make an important practical contribution to family planning in Latin America.

11. PAHO-coordinated pathology training program in Latin America

A 1965 survey of 27 pathology departments in general or university teaching hospitals in 8 Latin American countries showed that (1) the concept of clinical pathology did not exist in the hospitals; (2) almost all the departments were short of standard pathology textbooks and journals; (3) there was a need for coding and retrieval of autopsy and surgical pathology data.

On the basis of these findings the Pan American Health Organization and several interested bodies have been striving to improve the training and practice of pathology in Latin America. Special attention has been given to the distribution of reference and teaching material.

As a result of meetings with leading Latin American pathologists, members of the American Society of Clinical Pathology have begun donating pathology textbooks written not more than 6 years ago to various Latin American pathology departments to build up their basic specialized reference collections. The Pan American Health Organization receives the books, studies their suitability for pathology training programs, catalogs them, and finally forwards them to the countries of the Region.

The distribution of both current issues and bound volumes of past numbers of pathology journals in Latin America has made rapid progress, and the PAHO Regional Library of Medicine and the Health Sciences (RLM) in São Paulo has been the focal point of this effort.

A practice of exchanging and distributing 35-mm color pathology transparencies began in Brazil, Ecuador, and Mexico with the participation of the National Medical Audiovisual Center in Atlanta, Georgia. Since 1962 the World Health Organization has issued 10 publications in English,French, and Spanish dealing with standardized tumor nomenclature. Each publication is accompanied by a collection of 35-mm transparencies for reference and teaching purposes. Many hundreds of these publications and slides have already been distributed in Latin America.

In 1973 a comprehensive 3-year pathology training program was organized in Mexico at the request of that country's Secretariat of Health, Social Security Administration, and National University. A 2-year postgraduate training program in pathology was established in Ecuador in March 1974. This program should have doubled the number of pathologists in Ecuador by 1976.

To make better use of autopsies and surgical pathology material, protocols have been developed and have been tested in Brazil, Colombia, and Ecuador.

PAHO in 1972 published the Portuguese version of the American Cancer Society's Manual of Tumor Nomenclature and thereafter began making the manual available without charge to pathologists in Brazil and Portugal. Copies of the Systematized Nomenclature of Pathology have been provided to pathology laboratories in Brazil, Ecuador, Mexico, and Peru.

Practical demonstrations of the use of this pathology coding system have been conducted in Brazil, Ecuador, Mexico, Peru, and Venezuela for interested specialists. The American Society of Clinical Pathology, the American Cancer Society, the International Academy of Pathology, the U.S. Armed Forces Institute of Pathology, and the Department of Pathology of the U.S. National Cancer Institute have helped provide support for these efforts.

PAHO has also edited a simplified Manual of Histotechnology in collaboration with the U.S. Armed Forces Institute of Pathology.

In the discussion members of the ACMR commended the work done by PAHO, but emphasized the continuing shortage of pathologists and pathologic technicians throughout Latin America. The total number of pathologists in the subcontinent is estimated to be 1,200-1,500, compared with 12,000 in the United States. Ministries of Health give a low priority to this subject. It was noted that the PAHO fellowship program, over the last few years only 0.5 percent of fellowships have been requested for training in pathology. A major difficulty is that because of the low salaries the majority of pathologists work only part-time. To increase the number of trained people will be of little value without an adequate career structure of full-time posts.

While recognizing the very great difficulties of this problem the ACMR requested PAHO to continue to press governments to increase support for pathologists who, in modern medicine, form an essential component of the health team.

12. The PAHO Research Grants Program

As a result of a 1968 survey of 100 medical institutions and clinical departments in 9 Latin American countries, and at the recommendation of the seventh PAHO/ACMR, a pilot program for advanced training in clinical research was developed with funds from the Wellcome Trust matched by the Pan American Health Organization. Through this program, which aimed at taking advantage of the training potential of research institutions in Latin America and the Caribbean, the Secretariat communicates directly with the candidate scientists and institutions, and grantees are being selected on the basis of their ability, as appraised by a panel of scientists competent in the field of the proposed studies. Twenty-three training grants have so far been awarded to applicants from 12 countries for studies in cytogenetics, electron microscopy, endocrinology, hematology, immunology, nutrition, pathology, and perinatology. An additional program is being set up with the Wellcome Trust for the support of research training in England.

As a consequence of the encouraging developments in the research training program, the effort was extended to include support for research projects and for the exchange of research workers. Additional funds from PAHO's regular budget were allotted to the expanded program.

Preference is given to projects that attempt to solve problems of special importance for Latin America, and to applicants who are nationals of member or participating governments of PAHO. The focus, however, is on the support of people rather than of projects. Research grant applications are appraised for scientific merit by an in-house review procedure that involves the technical department concerned and the office of advanced studies in health, and up to three outside referees chosen from appropriate panels representing the main areas of PAHO's program activities. Since January 1973, 57 grant applications from 14 countries have been received. Thirty-six of these have been awarded, 14 are pending, and 7 have been rejected. The average sum granted is $5,000. It is intended to complement larger financial efforts made by the grantees' own institution or laboratory.

The grants in the program for the exchange of research workers are made to enable investigators to pay short visits to scientists working in similar or related fields in other countries, to exchange views or discuss problems encountered in their own research or in the interpretation of the results, or to acquire a new technique. Although funds available from PAHO for research purposes have steadily increased, the Organization cannot, realistically, be expected to become a major source of financial support for research. Its role is rather to serve as a research catalyst and outside sources of support remain vital to this function. The program for research and technical training in the mycoses is an illustration of what the Organization can do with a modest investment to develop a comprehensive research and training effort in an important health field.

The total PAHO research program is, of course, much larger when all funds are included. The 154 research projects listed in Research in Progress 1974 reflect the breadth of the current program.

The ACMR expressed its satisfaction at the development of the research grants program and strongly endorsed the policy of supporting people rather than projects. It emphasized the catalytic effect of such grants which, by providing a needed piece of equipment or a regular supply of materials, may be extremely productive at modest expense. Of particular importance are grants to postdoctoral workers to enable them to get research going in their own countries after they return from training overseas, and to foreign scientists to enable them to work in the region for 1-2 years.

The review of Research in Progress 1974 was not discussed in detail, but the Committee noted with satisfaction the increase in number and scope of the research projects, and the success achieved in attracting support from outside bodies.

13. Strengthening of the Brazilian Biomedical Information Network

At last year's meeting of the Committee, a paper prepared by Dr. Martin C. Cummings, Director, and Miss Mary E. Corning, U.S. National Library of Medicine, announced plans for testing the MEDLINE system in Brazil, and establishing an audiovisual (AV) center at the PAHO Regional Library of Medicine and the Health Sciences (RLM) in São Paulo, Brazil. These plans are now being implemented with the financial assistance of the United Nations Development Program (UNDP), the Brazilian Ministries of Health and of Education and Culture, and the State of São Paulo. Continuing technical assistance is being provided by the U.S. National Library of Medicine.

Testing of MEDLINE started in March 1974 with on-line operation of one and later two terminals colocated in São Paulo with an IBM 370/155 computer leased part-time from the State of São Paulo's Atomic Energy Institute. This test is now being extended to a four-city experimental network, São Paulo-Brasília-Recife-Rio de Janeiro, that will provide direct on-line access to the data base at São Paulo, 1 hour per week,

time-shared by the users. In a second phase, the MEDLINE system will be further deployed to 10 other cities of Brazil extending from Belém in the North to Porto Alegre in the South. Communications, in the form of asynchronous data transmissions at rates of from 110 to 1200 bps, will use the Brazilian voice network consisting of intercity microwave channels and urban telephone lines. This deployment is expected to be completed in 1975.

Cost of MEDLINE service will be substantially reduced when time-shared data communications become available in Brazil, possibly by 1976.

Extension of MEDLINE beyond Brazil is expected to be initiated experimentally and under separate funding in late 1974 or early 1975. This will involve a single point-to-point voice channel with multiplexing if several terminals are required.

In the audiovisual field, RLM's mission includes the acquisition, reproduction, and distribution of material, but not its production. RLM will also be responsible for training others in the use of audiovisual aids, assistance in selection of equipment, planning of audiovisual facilities, and management of multimedia learning and information programs.

The available equipment makes it necessary to limit and standardize the teaching material. Selection is initially concentrated on educational requirements in close coordination with the work of the Centro Latino Americano de Tecnologia Educativa para la Salud (CLATES/PLATES) groups. Assistance in selection is also provided by the Brazilian Association of Medical Schools.

Several organizations are contributing audiovisual materials to RLM, most notably the U.S. National Library of Medicine from its extensive collections at the National Medical Audiovisual Center at Atlanta, Georgia.

Some members of the Committee were concerned that this system of information retrieval may be over elaborate in relation to other research facilities in many centers in Latin America. The problem of scientific isolation cannot be overcome unless the MEDLINE system is supplemented by a program of building up local libraries in the places where the

terminals are. Such a library augmentation program has in fact been in effect for several years in the very libraries which will receive MEDLINE service.

The Committee considered that the parallel activity of the RLM in the selection and distribution of visual aids is of very great importance, because of the increasing pressure of student numbers.

14. Symposium on the role of schools of public health in the development of health care in the Americas

The issues summarized below were presented to the Committee but were not debated.

The session was almost unique, in that a wide subject dealing with delivery of health care, education, and the application of knowledge and skills to community health problems was being discussed at a research meeting. It was felt that the main functions of schools of public health were not only the traditional ones--education, research and service--but now must include orientation of public policy towards the delivery of health care and the development of health programs and services. Schools of public health are unique in their multidisciplinary character. Traditional medical schools, even with an expanded program, a wider interest, and greater sensitivity to the needs of the community cannot respond adequately to the total health of the public or community. Health cannot exclusively be the responsibility of the physician; it also depends on other health profession members who work together as a health team.

Schools of public health have not only an interdisciplinary team, but also an interdisciplinary student body, and provide the opportunity for the team to work together not only as teachers and students but in research, service, and consultation.

It was felt that in some respects the activities of schools of public health are too narrowly limited, and there is need to widen their scope so that they may become more effective. One of the main priorities

for the future should be to prepare professionals capable of detecting early problems of ill health and deviations from normal, so that effective preventive measures may be instituted as soon as possible.

A general view of the Region's health problems and the facilities for training in public health shows that there are still large numbers of people, especially in remote rural areas, for whom there is inadequate health care. This deficiency still exists, in spite of an increased number of medical schools over the years. New public health courses have been developed in Latin America and the Caribbean, where many persons are trained in their local settings to meet the peculiar health needs of their countries, but these courses are still too few.

An important element in training is to understand the mechanisms that govern health personnel policies, including planning, and to review the various functions necessary for change. Schools of public health have an important role in promoting changes in the health system, through revision of their traditional responsibilities and participation in a coherent political effort.

In considering the responsibilities of the schools of public health and the effectiveness of the health care system, it was recognized that the kind of change to which the schools are committed cannot take place unless the diverse influences in society, which affect health and programs to promote it, are acknowledged and dealt with in an integrated way. Training for leadership is a major goal. Personnel thus trained should have the knowledge and skills necessary to define health problems. They should also have the ability to educate the general public so that it understands the various issues, and accepts the approach being made to the solution of the problems. There should be opportunity for faculty and students to be involved practically in the health problems of the state or nation. There should be interaction at the level of both policy and delivery of care. Many public health schools have a close relationship with the ministry of health of the country in which they are located, and this relationship is beneficial to both school and ministry. From the point of view of the school, it provides an excellent opportunity

for the faculty and students to become directly involved in field health activities. From that of the ministry, it yields the benefits of the special knowledge and skills of the school.

Interest in public or community health is increasing, as many people are emphasizing more and more the importance of man in his total environment. Schools of public health are therefore urged to be active in defining needs (including the expectations of the public, health professions, governments, and other agencies); in studying and proposing ways to improve the existing health status of people and communities; and in monitoring and evaluating the extent to which objectives are being met. They also play an important role in the training and continuing education of many types of health personnel at all levels.

The use of modern communication techniques in health education is important. There should also be a closer relationship between the health and social services at the national level. It is likewise important that there should be a dynamic interaction between medical and postgraduate schools, and continuing education should have a higher priority. Schools of public health have a major role to play in all these situations.

There is at present some confusion as to what is meant by public health, community health, social medicine, social and preventive medicine, and community medicine. The widest term, public health--the health of the public or community--would in this context include concern for such diverse things as: the supply of potable water to communities; the reduction in or prevention of automobile accidents; the increasing world-wide problem of venereal diseases, etc. Schools of public health have a vital role to play in this area. They should be given all possible assistance to meet their wide and important responsibilities for the health of the several nations.

To meet the increasing demand for teaching staff in a wide range of health disciplines, training institutions, particularly medical schools, have started postgraduate education in several subjects. The departments of social and preventive medicine or community medicine in many schools have provided postgraduate training courses in public health. This

approach, using limited available resources, is complementary to the restricted possibilities for training offered by the existing schools of public health.

In summary, participants agreed that health care involves to a very large extent the entire community, and universities must participate in it. Because of the small number of schools of public health, it will be necessary for schools of medicine to assist in training public health personnel to work for governments, who are the chief consumers. There is a need to improve training, as public health officers must assume greater responsibility for health care in the society.

Research must be executed at all levels and should be of such a nature as to influence social development and changes in government policy. Trained public health officers should be competent to evaluate the community's health status and to facilitate the team approach to health problems.

Health education in its broadest sense must be one of the major aspects of public health training. This would include community participation so that attitudes may be changed. Teachers in schools of public health must be involved in active service to health departments and in the community so that teaching is relevant to its needs and practices. Schools of public health can truly be interdisciplinary centers for orienting government policy and social change for the benefit of our communities.

15. Symposium on ecology and pollution in the Americas

The opening statement of the moderator appears in full in the appendix.

Rapid population growth, industrialization, unplanned land use and urbanization are creating unprecedented impacts on man's environment. The speed, magnitude and complexity of these forces intensify

traditional problems and create new stresses. The gap between the diagnosed and the undiagnosed health implications of environmental changes is widening.

The broadening dimensions and the rapidity of change impel health and other agencies, active in environmental matters, to assess health impairments and to measure, quantitatively, wherever possible, the impacts of environmental conditions on the physical and mental well-being of man.

The health achievements of this century have been great in reducing infant mortality and gastrointestinal diseases and are well documented. A tremendous task remains in the improvement of the environment to provide better protection to the millions still living under insanitary conditions characteristic of underdevelopment. The traditional absence of basic sanitation and the consequent associated diseases remain a very large challenge.

A characteristic of the present age is the rate at which man is modifying his own environment, so that industrial and chemical hazards have been superimposed on the classical ones. At the present time, among the chemicals considered most important as environmental hazards, are NO_2, nitrates and nitrites in food giving rise to nitrosamines, mycotoxins, manganese, organic chlorine compounds, asbestos, and others. One of the most distressing features of modern industrially produced hazards is the long-time lag between exposure and effect. Asbestos provides a good example of the time required for induction of disease. The time lag for the production of fibrosis alone may be as much as 20 years. After that lapse of time the incidence and severity increase rapidly. A distinction has to be made between the time since initial exposure and the duration of exposure. More recently an association has been established of asbestosis with cancer of the lung and mesothelioma. There has been a spectacular increase in the incidence of these conditions in asbestos workers after 20 years from first exposure, and even quite small exposures can result in mesothelioma.

Asbestos may be an illustration of another aspect of the problem of environmental pollution. Because of the wide use of asbestos in modern industrial processes, the hazard affects not only those who are occupationally exposed, but a wide range of workers and indeed the community generally. Asbestos bodies have been found at autopsy in the lungs of people who have had no occupational exposure. Community sources of exposure include mine dumps, road coverings, brake linings, some items of clothing, construction, demolition, spraying of insulation and pasting of dry walls. Air samples are positive for asbestos in all American cities examined.

If the risks of industrial development are to be weighed against its benefits, it is necessary to define what constitutes a hazard.

Attention was drawn to the tentative nature of information on which criteria are based. Even those for ionizing radiation, on which most work has been done, are now under attack. The operation and effects of chemical agents can be quite complex. The concept of a threshold level below which there are no effects presents many difficulties. The time lag is also a particular difficulty; an effect not demonstrable today may show up many years from now. Individuals vary in their ability to repair damage and in their susceptibility. We can never say with certainty that a particular substance is nontoxic.

Priorities for consideration have been set up and procedures are being established by the World Health Organization for the establishment of criteria. The final answers will be different for different countries and different situations. An early warning system for acute and chronic effects is needed. Conventional national statistics are not very useful; information is often lacking on the most important points. Trends in large population groups must be watched. Chromosome breaks, cancer registries, congenital malformations, blood enzymes, antibody titers, and nutritional indices can provide information for detecting shifts in health. For these, a central data-handling facility is needed.

Significant advances have been made in the Region over the last few years in preserving and improving the quality of the physical environment.

Public awareness of environmental problems, the promulgation of specific laws and regulations, and the creation of new environmental agencies have made it possible to accelerate the assessment of environment pollution and to initiate control programs. Several universities have devoted considerable attention to the environmental sciences, have provided training in new disciplines, and have offered new relevant courses.

Short courses, seminars, and symposia on environmental matters have proliferated. Research on environmental pollution has progressed but still needs amplification. Research projects have been carried out on the effects of atmospheric pollutants on human health, in development of low cost technology for treatment of municipal sewage and industrial wastes, on studies of water quality, and on characteristics and treatment of urban solid wastes.

Latin American and Caribbean countries can profit from the experience of the more developed countries in environmental management. Preventive measures, utilizing the experience of developed countries, can avoid unnecessary economic and social costs, and reduce damage to natural resources.

Many different ecosystems abound in the Region, with different problems requiring different solutions.

In response to this need, in October 1971 the PAHO Directing Council urged member countries in Resolution XXXI to strengthen their capabilities to cope with health problems related to the changing human environment, and requested the Director to explore means for the establishment of a Center for Human Ecology and Health Sciences.

The Committee heard a preliminary report on a proposed plan for the Center:

A Center for Human Ecology and Health Sciences would provide a mechanism for the understanding of the complex interrelated phenomena underlying the human body's reactions to the increasingly wide range of environmental hazards--biological, chemical, and physical.

To accomplish its tasks the Center will include a wide range of competence in such fields as environmental toxicology, environmental physiology, bioengineering, molecular biology and cytology, epidemiology, biomathematics, human ecology, analytical methods, and supportive services in pathology, computing, and information handling.

Further, the Center will collaborate closely with PAHO's existing network of centers, and in particular it will complement the physical sciences and engineering activities of the Pan American Center for Engineering and Environmental Sciences in Lima as a resource in the biological sciences and medicine.

The Center's suggested objectives are:

1. To develop biomedical and epidemiologic methodology to identify, define, and monitor health problems of environmental origin;

2. To advise governments on programs and actions to minimize the adverse effects of the environment on health;

3. To conduct and support training of environmental health specialists;

4. To conduct, support, and promote research; and

5. To provide information for global assessment of health problems of environmental origin.

Development is expected to proceed along five lines:

1. Creation of a technical information base.

2. Identification of major environmental problems.

3. Provision of advisory and consultative services.

4. Participation in training of environmental health personnel.

5. Organization and conduct of applied research.

Arrangements are being made to hold a seminar in September 1974 in order to define more clearly these suggested objectives and ideas. The establishment of this Center in Mexico will make a very great

contribution to solution of some of the problems which have been touched upon in the Symposium.

To cope with both the traditional and the emerging environmental problems, the developing countries must have available the scientific knowledge and the technology which the more advanced countries have developed and applied. The technology, however, must be adapted to local conditions and resources.

Present deficiencies in research may be listed, as follows:

1. Research efforts are still very unevenly distributed throughout the Region.

2. Although research, mainly applied in nature, is being carried out in some countries, the results are not adequately distributed.

3. A strategy for research in environmental problems needs to be developed, according to the priorities of the individual countries. Duplication should be avoided, at least for the time being, by improved communication between investigators, institutions, and government.

4. Training of researchers should receive special attention.

5. Research in environmental subjects should be largely "problem oriented" to provide urgently needed solutions to real and pressing needs.

6. The multidisciplinary nature of solutions to environmental problems imposes upon health agencies the necessity to collaborate with other groups active in pollution abatement.

7. Emphasis should be given to investigations where direct correlation between contaminant and human health is suspected, but not yet clearly established.

8. Research in environmental matters should be especially oriented to develop better and more economic technologic solutions to traditional as well as to emerging problems.

The Committee considered that PAHO, mainly through its Centers, should provide scientific and technologic research assistance to member countries in matters of environmental protection and control.

In the discussion on the papers presented the ACMR noted the very serious technical problems involved in monitoring the effects of environmental pollution. It was suggested that two approaches are possible: to identify a process and watch for effects in those exposed; or to take a harmful effect and follow it back to a possible causative agent. As an example, regional differences in the incidence of tumors should provide clues to their causes.

Another difficulty is to find the right balance in the approach to these problems. In the present stage of development of Latin America, infection and hazards of industrialization seem to lie at opposite ends of a scale, and the significance of industrial hazards for the general mass of the people may be questioned. Even if the risks at present are not widespread, the important point is to look to the future.

It was noted that the effects of pesticides used for spraying crops have not been considered in the Symposium, but the Committee was informed that there is no evidence as yet of health hazards from this source.

In conclusion, the point was made that support for research will not come unless scientists and health workers convince the authorities that these problems are important and that they can be prevented.

The Committee expressed their thanks to all those who had organized and taken part in this Symposium, which had focused attention on an area of great concern and had provided a valuable outline of what is being done and what needs to be done.

16. Immunology of Chagas' disease

The Committee reviewed the memorandum summarizing the current status of the immunology of Chagas' disease, prepared on the occasion of the meeting held in December 1973, at the Immunology Department of the National Nutrition Institute in Mexico.

A number of findings indicate that a careful study of a variety of immunologic factors may be very important for a better understanding

of Chagas' disease. Eventually this knowledge will be useful not only to throw light on the host-parasite relationship but also for diagnostic, epidemiologic, and control purposes.

Among other questions to be answered are the possible antigenic variations in different strains of the parasite, the exact role of cell-mediated immunity, and the possibility of the occurrence of auto-immune reactions. These variables should be correlated with the different clinical pictures of the infection.

During the discussion it became evident that longitudinal studies of persons infected with T. cruzi, such as the one just began in Bahia, should be pursued for at least 10 years. This knowledge is essential to evaluate the economic impact of the disease. In addition, a thorough assessment of the impact would be helpful for the funding of research.

To achieve a better knowledge of the immunology of Chagas' disease it is essential to organize adequate communication between scientists engaged in that type of research. In addition, it is necessary to standardize reagents and techniques and to develop the necessary reference centers, both at national and international levels.

The need to pursue studies that may eventually lead to the development of a vaccine was also emphasized.

The Committee discussed the multidisciplinary activities that should be undertaken to deal with different aspects of Chagas' disease. Work on immunology and host-parasite relationships should be complemented by further studies of vector ecology, and of prevention methods by the improvement of housing.

Finally, the Committee stressed the importance of the human infection with T. cruzi, which affects millions of individuals. This underlines the need not only for more basic research on this parasite--and indeed on parasitic diseases in general--but also the need for action, that is, application of available knowledge to the prevention of Chagas' disease.

In this context there was some debate on the type of research which should have a high priority in Latin America. It was agreed that centers in the region have an inescapable responsibility to promote research which, for geographical reasons, cannot be conducted elsewhere.

17. Third Meeting of the Scientific Advisory Committee on Dengue

The Committee received the full report of the Third Meeting of the Scientific Advisory Committee on Dengue, held in Bogotá on May 21-23, 1974. This body was organized by PAHO in 1970 with the main objective of furnishing advice, in view of the increased activity of dengue virus and the possibility of the occurrence of dengue hemorrhagic fever (DHF), including shock syndrome, in the Americas.

Dengue continues to be prevalent in the Western Hemisphere and the recent outbreak in Colombia with 450,000 cases, as well as the marked activity of the virus in Puerto Rico, indicate the regional importance of the disease, which traditionally has produced large and explosive epidemics in different countries of the world infested with Aedes aegypti.

The ACMR expressed its concern over the situation. The latter does not show signs of improvement because of the problems, particularly administrative and financial, which make elimination of the vector difficult. As a result, the risks of DHF and urban yellow fever continue to be serious.

The ACMR noted the efforts of PAHO in helping in the disease surveillance, strengthening the laboratories located in the endemic areas, and in general, in the implementation of the recommendations made during the early meetings of the Committee on Dengue. Such recommendations included the editing of the Dengue Newsletter, the distribution of reagents, and the workshop held in Puerto Rico regarding new techniques for the diagnosis of the infection.

The ACMR reviewed the Committee on Dengue's recommendations for research and expressed agreement with them. These recommendations include the strengthening, improvement, and extension of the current surveillance systems, studies of biologic differences among dengue virus strains, research on the ability of A. aegypti in various geographical areas to transmit dengue and yellow fever and comparative histopathologic studies of the liver in persons dying from either of these diseases. The latter study could be organized by PAHO with the participation of recognized authorities in the field, using coded specimens and suitable controls. A major recommendation of the Dengue Committee, which was endorsed by the ACMR, was that it be reconstituted to include persons competent in the fields of both dengue and yellow fever viruses and persons knowledgeable in vector biology and control.

The ACMR reviewed the present situation on dengue vaccine research. The development of live-attenuated dengue virus vaccines is considered an appropriate research effort at this time. The feasibility of developing suitable attenuated virus strains has been established with reasonable certainty. Major constraints on vaccine development were identified; these include lack of virologic knowledge, inadequate markers of virus virulence, limited cell culture substrates for vaccine production, and genetic instability of attenuated strains.

During the discussion the need became evident to improve the viscerotomy services in the Americas and to improve the technique for obtaining specimens.

The ACMR fully agreed that in view of the constant dangers of dengue and yellow fever the most important action to take is to concentrate efforts on the eradication of A. aegypti.

18. Topic of the Special Session for the 14th Meeting

The Committee debated briefly the general principles on which this session is organized, and in particular on what occasions the

topic should be chosen by the Committee itself, or by the PAHO secretariat, or by both.

The majority opinion with which the Director concurred, was that the onus was on the Committee to decide on the topic and to organize the session, since it is the responsibility of the Committee to indicate to the Organization areas of research which it feels are relevant to the health problems of Latin America.

After this discussion the ACMR accepted a proposal by Professor Carlos Chagas that the topic for the Fourteenth Session should be: "Urbanization, internal migration, and the spread of disease."

It was considered that an important topic for a future session would be "pre- and post-natal factors affecting child mortality."

The Fourteenth Meeting of the PAHO Advisory Committee on Medical Research has been tentatively scheduled for 30 June - 4 July 1975.

APPENDIX

SYMPOSIUM ON ECOLOGY AND ENVIRONMENTAL POLLUTION

Moderator's Opening Statement*

Exactly 10 years ago, this Committee held a 1-day session devoted to discussions of "Environmental Determinants of Community Well-Being". The subject matter covered a broad spectrum of environmental issues ranging from an appraisal of those influences, via epidemiologic methods, to delineation of such specific problems as housing and their service utilities. Throughout the deliberations, the significance of social and cultural impacts was stressed. Even then, the ecologic approach to the problems of community well-being dominated the exchange of ideas.

The practical issues, still confronting us today, were not lost sight of, while pursuing the ethics and morality of man vis-a-vis nature. In a summary of the session of a decade ago, the late Dr. Anthony M. M. Payne posed the dilemmas of a health officer in the following terms:

"In Latin America millions of people span, in effect, two centuries of cultural and political contrasts. How can these gulfs be bridged in terms of the provision and acceptance of modern sanitary measures? What are the priorities in the face of limited resources and rising expectations? And, finally, what are the areas of ignorance that must be illuminated to facilitate the actions of tomorrow?"

Although a great deal of progress has been made in some areas of environmental concern and correctives, since those questions were posed, it is disconcerting to note that similar issues still confront us. Run-away population growth, astonishing urbanization and vast

*Dr. Abel Wolman, Emeritus Professor, The Johns Hopkins University, Baltimore, Maryland.

industrialization dramatize and intensify the issues of 10 years ago. The primary causes of mortality and morbidity are still, to a significant degree, environment-borne.

For our demographic setting, we have today some 318 million people and a dismaying prospect, in the year 2000, of 650 million souls. There is no average country or even average region in any given country. Within a single area, vast differences occur in density of living, occupation, income, social organization, and attitude. Decision-making, therefore, runs the risk of overgeneralization or even overphilosophizing as to appropriate strategies for corrective measures.

In our recent semantic enthusiasms regarding man and his ecologic stance, some thoughtful people have pointed out that "one hallmark of contemporary America--is the short life span of its crises.---Civil rights, urban decay, hunger, drugs, crime, campus unrest, medical care, the environment, energy---one succeeds another with blurring speed, almost as though some issue-of-the-year club were in charge."[1]

Fortunately, or unfortunately, in Latin America, most of these issues have always been with us, buffeted, however, by the same ephemeral winds of doctrine as in North America. The challenges to the Central and South American ministries are in their capacities to distinguish between the actual and the possible, between the present and the prospective, and between the known and the unknown hazards to life and well-being in the environment.

The simplest task of all is to list the ingredients in the environment, whether biological, chemical, physical, economic, political, or social. This shopping list is then expanded to suggest the relative hazards they may singly and collectively pose. The obvious epidemiologically validated facts are coupled with the subtle, intriguing potentials in the remote future. Much of recent literature on environment and health covers the real hazards as well as the enticingly unknown. Where knowledge

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[1] A. L. Otten, Wall Street Journal, 6 May 1974, p. 16.

of cause and effect is inadequate, as it often is, the reality of threat is frequently tenuous. The suggestion to seek more knowledge is always unpopular. Hence, the temptation is to try drastic action, or else to do nothing, which is almost as bad.

In the present climate of public opinion, a minister of health is further plagued by the feeling that he should also be conservationist, preservationist, and overall protector of the biosphere. If we add to these functions, family planning and zero population growth, he will be so weighted down that his original responsibility for the prevention of disease and the promotion of health declines.

He cannot escape the necessity of continuity of surveillance, the assessment of prevailing and frank disease, the detection of new threats, and the illumination of choices of action. Now, he is torn from pillar to post by popular, and often misguided demands. Can an advisory board lighten this burden, by a renewed interest in the environmental domain here discussed, by expanded inquiries into the unknown, and by the epidemiology required to separate the "wheat from the chaff" in health department activity?

The universality of the enteric diseases in the Americas must somehow be weighed against such environmental hazards as mercury poisoning. The former phenomena are too familiar. The latter was the temporary "pitch" of the mass media. The diarrheal diseases have posed a serious and constant problem, for over a century.

After an absence of half a century, Shigella dysenteriae, type 1, reappeared in Belize, Costa Rica, El Salvador, Guatemala, Honduras, Mexico, and Nicaragua. The epidemics simply dramatized the fact that millions of people consume human fecal material all their lives, and that diarrheal diseases still represent the first or second cause of death.

Similarly, the recrudescence of thousands of cases of typhoid fever in Mexico in recent years, reminds us that a world presumably made safe by antibiotics, therapeutic chemicals, and less than effective

vaccines, is not so safe. The fecal-oral route has not been eliminated, but was merely ignored.

One may hope that out of today's discussions some light will emerge as to how PAHO is to make its way in leadership through the shoals of environmental impact upon man. Every day the Organization must take its multiple choice examination. It must do something of everything, but it must recognize that some objectives are far more important than others.

Are nearly 200,000 cases and over 11,000 deaths from Shigellosis in El Salvador (July 1969 to June 1973), and 12,000 excess deaths--diarrheal and dysenteric--in Guatemala, in the last several years, as important as the rare human cases of mercury poisoning? Is the choice to be made by television coverage, because of the tragic experience with mercury in Japan, caused by inexcusable industrial practices? Or can it be made, at least in part, on the basis of the best information and warrant?

PAHO must and will concern itself with the vulnerability of the fetus and the child to chemical pollutants. It cannot escape the gnawing responsibility for research in the mutagenic and carcinogenic risks inherent in the environment.

Can it profit by a deliberate epidemiologic investigation as to whether the millions of cases of Chagas' disease might be materially reduced by economical surfacing of the walls of houses, so as to eliminate the harborage of the vectors of this disease? Would this be far cheaper than the specter of building anew hundreds of thousands of houses?

How much metahemoglobinemia of infants actually occurs in the Americas because of excessive nitrates in drinking water? Is its frequency so great that it warrants rigid prohibition of the use of such waters? If not, why the costly vigilance?

Is noise a major public health hazard, other than in industry? How much budgetary allotment should go into control of "rock-and-roll"

music, or the air compressor? These questions are all relevant to decision-making--and incidentally to this Advisory Committee's interests and functions.

A director of health must practice selection in his strategy of work, as well as in his devotion to studies. His resources, as well as those of all other ministries, are always in short supply. They must not be squandered, while in the pursuit of knowledge or seduced by the interesting, but unimportant. Obviously, no public servant can be impervious to public clamor, no matter how erroneous. He should, however, strive to lead as well as to follow.

The discussions today continue to pursue answers to the central questions posed by Dr. Payne 10 years ago.

Pan American Health Organization

THIRTEENTH MEETING OF THE
ADVISORY COMMITTEE ON MEDICAL RESEARCH

Headquarters Building
Conference Room B
Pan American Health Organization
525 Twenty-third Street, N.W.
Washington, D.C.

24-28 June 1974

AGENDA

Monday
24 June

9:00 a.m.	1.	Opening of the meeting - Chairman (5 min)
9:05	2.	Introductory statement - A. Horwitz (10 min)
9:15	3.	Control of disease in Amerindians in cultural transition - J. V. Neel (20 min)
9:35		Discussion (15 min)
9:50	4.	The mycoses as a potential public health problem in the Trans-Amazon Highway region - L. Ajello (20 min)
10:10		Discussion (15 min)
10:25	5.	Sporozoite-induced immunity in mammalian malaria - R. Nussenzweig (20 min)
10:45		Discussion (15 min)
11:00		C o f f e e
11:15	6.	Progress report from the Chagas' Disease Research Unit in Salvador, Brazil - D. M. Minter (20 min)
11:35		Discussion (15 min)

11:50 a.m.	7.	Mycobacterium ulcerans in the armadillo - D. H. Connor/R. E. Krieg (20 min)
12:10 p.m.		Discussion (15 min)
12:25		L u n c h
2:00	8.	Dental caries in Colombian communities - B. Cohen/ W. H. Bowen (20 min)
2:20		Discussion (15 min)
2:35	9.	Manganese poisoning: a metabolic disease of the brain - G. C. Cotzias/I. Mena (20 min)
2:55		Discussion (15 min)
3:10	10.	Research needs in areas of high natural radio-activity - M. Eisenbud (20 min)
3:30		Discussion (15 min)
3:45		C o f f e e
4:00	11.	Considerations in the protection of humans as subjects of research - D. T. Chalkley (20 min)
4:20		Discussion (15 min)

Tuesday
25 June

9:00 a.m.	12.	PAHO/WHO expanded program on research and training in human reproduction - J. Rosner (20 min)
9:20		Discussion (15 min)
9:35	13.	PAHO-coordinated pathology training program - H. Torloni (20 min)
9:55		Discussion (15 min)
10:10		C o f f e e

10:30 a.m.	14.	PAHO research grants program - M. Martins da Silva (15 min)
10:45		Discussion (15 min)
11:00	15.	Strengthening the Brazilian biomedical information network - J. D. Wilkes (20 min)
11:20		Discussion (15 min)
11:35		L u n c h
2:00 p.m. to 5:00 p.m.	16.	Symposium on the role of schools of public health in the development of health care in the Americas - Moderator: M. E. Wegman (for details, see page 8)

Wednesday
26 June

9:00 a.m. to 5:00 p.m.	17.	Symposium on ecology and pollution in the Americas - Moderators: A. Wolman and J. J. Hanlon (for details, see page 10)

Thursday
27 June

9:00 a.m.	18.	Reports of scientific meetings and symposia
	18.1	Immunology of Chagas' disease - G. Torrigiani (20 min)
9:20		Discussion (15 min)
9:35	18.2	Third meeting of the scientific advisory committee on dengue - P. K. Russell (20 min)
9:55		Discussion (15 min)
10:10		C o f f e e
10:30	19.	Selection of topics for the special session of the fourteenth PAHO/ACMR meeting

11:00 a.m.	20. Other matters
11:30	L u n c h
2:00 p.m. to 5:00 p.m.	21. Preparation by the rapporteurs of the meeting's report

Friday
28 June

9:00 a.m.	22. Committee's recommendations
12:00 noon	23. Closure of the meeting

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THIRTEENTH MEETING OF THE
PAHO ADVISORY COMMITTEE ON MEDICAL RESEARCH

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24-28 June 1974

AGENDA

SYMPOSIUM ON THE ROLE OF SCHOOLS OF PUBLIC HEALTH
IN THE DEVELOPMENT OF HEALTH CARE IN THE AMERICAS

Moderator: M. E. Wegman

Tuesday
25 June

2:00 p.m.	1.	Introductory remarks - M. E. Wegman (5 min)
2:05	2.	Health problems in the Region and the training in public health - J. R. Teruel (10 min)
2:15	3.	Preparation of human resources and health care needs - A. Neri (20 min)
2:35		Discussion (30 min)
3:05		C o f f e e
3:20	4.	Public health schools and health care system effectiveness - C. G. Sheps (20 min)
3:40		Discussion (30 min)
4:10	5.	Provision of health services: public and health agency expectations - J. E. F. Hastings (20 min)
4:30		Discussion (30 min)
5:00	6.	Concluding remarks - M. E. Wegman (10 min)

SYMPOSIUM ON THE ROLE OF SCHOOLS OF PUBLIC HEALTH
IN THE DEVELOPMENT OF HEALTH CARE IN THE AMERICAS

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24-28 June 1974

AGENDA

SYMPOSIUM ON ECOLOGY AND POLLUTION
IN THE AMERICAS

Session I

ENVIRONMENTAL POLLUTION

Moderator: A. Wolman

Wednesday
26 June

9:00 a.m.	1. Introductory remarks - A. Wolman (10 mins)
9:10	2. Environmental pollution problems in Latin America - O. A. Sperandio (20 min)
9:30	Discussion (10 min)
9:40	3. Economic and social aspects of environmental pollution - E. R. Yassuda (20 min)
10:00	Discussion (10 min)
10:10	4. Health aspects of environmental pollution - D. I. Hammer - (20 min)
10:30	Discussion (10 min)
10:40	C o f f e e

11:00 a.m.	General discussion
11:30	Summarization - A. Wolman
12:00 noon	L u n c h

Session II

HUMAN ECOLOGY AND HEALTH

Moderator: J. J. Hanlon

2:00 p.m.	5. Introductory remarks - J. J. Hanlon (15 min)
2:15	6. Environment and human health - I. J. Selikoff (25 min)
2:40	Discussion (10 min)
2:50	C o f f e e
3:10	7. Environmental health criteria and early warning systems - M. Kaplan (30 min)
3:40	Discussion (10 min)
3:50	8. Proposal for a regional center on human ecology and health - D. H. K. Lee (20 min)
4:10	Discussion (10 min)
4:20	Open discussion
4:50	Summarization - J. J. Hanlon

SYMPOSIUM ON ECOLOGY AND POLLUTION
IN THE AMERICAS

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