Pan American Health Organization World Health Organization

XVI Pan American Sanitary Conference

XIV Regional Committee Meeting

Minneapolis, Minnesota, U.S.A.
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RESEARCH PROGRAM

DIRECTOR'S REPORT ON PAHO RESEARCH POLICY AND PROGRAM

During the Quadrennium just ended and in the first six months of the present year, there have been significant developments in the medical research program of the Organization. The research program was undertaken in the light of the basic objectives of the Organization as stated in Article 1 of the PAHO Constitution:

> "The fundamental purposes of the Pan American Health Organization shall be to promote and coordinate efforts of the countries of the Western Hemisphere to combat disease, lengthen life, and promote the physical and mental health of the people."

In recognition of the purposes of the Organization and of the growing importance of research as an essential component of a comprehensive program for the betterment of health in the Americas, and as instructed by Resolution XXXVIII of the XIII Meeting of the Directing Council (Washington, D. C., October 1961) (see Annex I) studies have been undertaken to guide an expanded and intensified research and research training effort to solve health problems for which there are presently inadequate or no available answers. As the program develops it will be related to the distinctive needs and opportunities for research existing within the Member Countries. It will emphasize research projects requiring coordinated effort by more than one country and research activities that will stimulate a wider application of existing and new knowledge to the special problems of each country. In addition to the great and growing resources of the Americas, PAHO will draw upon the diversified experience of the World Health Organization. The research policies and programs of both Organizations will be fully coordinated, bearing in mind the opportunities and special needs and requirements of the Americas.

PAHO/USPHS Agreement

An important development of the Quadrennium which greatly strengthened the research activities of the Organization was the agreement announced jointly in December 16, 1960, between the Pan American Health Organization and the U. S. Public Health Service. The agreement (see Annex II) issued as a "statement of arrangements" between the two organizations, focused on three main points: (1) staff collaboration between the two organizations; (2) further development of PAHO research activities; and (3) definition of forms of USPHS aid that might be applied to PAHO research activities. Under the agreement, the USPHS will consider proposals for grants made by investigators who may wish to participate in research programs coordinated by the Organization, as well as applications for grants in support of research to be conducted directly by the staff of the Organization.

In line with this agreement, the Organization in 1960 encouraged the Bureau of Public Health Economics of the University of Michigan, to apply for a research grant from the National Institutes of Health of the USPHS, for a study of the economic implications of malaria eradication in the Americas, and pledged to make a supplementary contribution equal to 10 per cent of the amount granted by the NIH. Consequently, when a grant of US$95,000 was made by the NIH for a three-year study of the problem, the Pan American Health Organization provided US$9,500. This study is now in progress, with the Organization providing assistance in planning the field work and in selecting the areas to be studied.

Another example of effective collaboration under the agreement is the study of comparative mortality rates by causes in nine American cities, organized in 1961 by the Health Statistics Branch of the Organization, which promises to provide valuable data for future epidemiological studies on geographical differences in the distribution of fatal diseases.

Research and training activities are also expanding at the Institute of Nutrition of Central America and Panama, the Pan American Foot-and-Mouth Disease Center, and the Pan American Zoonoses Center. These programs are solidly founded on proved systems of international cooperation among interested countries. In each case PAHO provides administrative and logistic support and technical supervision. It is gratifying to note that these centers are attracting substantial voluntary grants on a mounting scale with which to expand their research efforts. The Organization thus serves its Governments by maintaining a relatively small central core of expert personnel who are able to attract the scientists and grants without which the difficult problems of malnutrition, foot-and-mouth diseases, and the zoonoses will not be solved.

It is evident that, as the research interests and activities of the Organization have expanded, an increasing responsibility has devolved upon Headquarters to provide sound policy guidance and logistic support for existing programs and to develop studies looking toward the solution of many other problems of an international nature not presently directly embraced in the Organization's program.

The Office of Research Coordination

Recognizing the Organization's need and its unique resources and objectives, and in the spirit of the agreement of December 1960, the USPHS National Institutes of Health made a grant of $120,750 in 1961 to permit PAHO to make the necessary studies to provide the basis for a sound, effective, and productive expansion of its research policy and program. To assist the Director and the technical branches of the Organization in carrying forward such studies, an Office of Research Coordination was created in late 1961. Among the subjects which have been identified thus far as requiring research and research training efforts on a more intensive and coordinated basis are: Arthropod-borne viruses, Chagas' disease, foot-and-mouth disease, leprosy, malaria, plague, and schistosomiasis. Wider areas where intensified research is required are the zoonoses in general, nutrition, dental health, radiation health, mental health, maternal and child health, environmental health, medical care, and health economics.

The present report, including the attached document (Annex III, RES 1/19) provides an overall appraisal of the existing research program and reviews a number of proposals for the expanded program. Expert consultants and staff specialists reviewed the status of knowledge in each field of subject matter, appraised the resources available for research, and suggested promising lines for further investigation.

The Report of the PAHO Advisory Committee on Medical Research

To assure the broadest and wisest possible consideration of these complex and difficult problems, the assistance of the PAHO Advisory Committee on Medical Research is invaluable. This group of twelve distinguished scientists, educators and administrators of the Americas convened in Washington for their first meeting from 18 to 22 June of this year to consider the reports and recommendations of the expert consultants and of our technical branches and research centers. The Committee's Report (Annex III, RES 1/19) and recommendations are transmitted herewith, including summaries of the documents which it reviewed, for the information and guidance of the Organization's Governments and of the Conference. In some instances, it will be noted that further studies are suggested and additional reports are called for.

In a fast-changing, interdependent world in which revolutionary advances in all branches of science and technology, not least in the bio-medical field, are the order of the day, the work of planning and coordination must proceed on a continuing basis. However, this report is made in the fullest confidence that the outlines of a long-term policy on research for the Organization have emerged and that, with the approval of the Conference, its Governments will be assured of an intensified and expanded program of research and research training with which they will wish to cooperate. While the Organization has demonstrated over the years that the pooling of resources in a concerted attack on unsolved problems is a very good method of getting results of benefit to all at a reasonable cost, in the longer run bio-medical research in the Americas can be no stronger than the research interest and resources of the Member Countries.

In this connection, the Advisory Committee report recommended (page 6, first paragraph) that,

> ". . .each country carry out, by means of . . . a National Research Council, or by some means, a radical study of the programs in the health and related sciences, so as to identify where research activities should and could be stimulated and career appointments be made to advantage. It was recommended that PAHO support these studies by offering the services of consultants."

Such studies would be invaluable to the Organization in shaping its program to meet the needs and opportunities of each country and of the Americas as a whole.

Definition of Research

In considering research broadly, the Committee made some illuminating observations on so-called "fundamental" and "applied" research, stating (page 1, last paragraph) that,

> "It felt that all genuine good quality research is fundamental if it contributes to the more complete understanding of the multi-faceted aspects of complex problems. This is particularly so when dealing with man, who is the central object of its concern."

The Committee observed further (on page 2) that,

> "Fundamental science is not distinguished by the use of mathematical, physical, or chemical methods per se, but rather by the relevance of the research to an intelectually and practically satisfactory solution of the problem at hand.
>
> The immediate purpose of supporting research in Latin America is to solve problems related to health in a manner which will promote human welfare. . . The long range goal is to promote the upgrading of the community in its most human aspects through the cultivation of science."

It was from this broad philosophical yet, at the same time, practical point of view that these distinguished leaders of science and public affairs approached their analysis of the subject matter in the documents, and their counsel was most helpful and always practical.

The Expanded Program and Research Priorities

The Committee reviewed research needs and recommendations for intensified efforts in the study of Chagas' disease, malaria, schistosomiasis, leprosy, plague, arthropod-borne virus diseases, and some of the zoonoses. It also considered reports and recommendations on the more general fields of environmental health, dental public health, maternal and child health, nutrition, radiation health, medical care, and health economics.

The Committee's analysis, priorities, and recommendations are being studied by the Organization in developing an action program appropriate to its resources. It is clear that the range and diverse character of the expanded program is such that it will take time to implement all of the promising lines of investigation suggested by the Committee.

It can be stated, however, that the Organization and its Governments now have in their hands a solid body of up-to-date knowledge about a wide range of research needs, urgent problems requiring solution, and promising lines for intensified research.

Concerning priorities, the Committee observed (page 3, last paragraph) that,

> "The basis for the establishment of priorities are several. The research project must be relevant to the field of health and it must somehow promise dividends in terms of new and significant knowledge and of increased human welfare. It is rarely possible to obtain an accurate idea of the economic importance of the problem to be studied, because of lack of data in this area. Since this important criterion could so rarely be used, research on diseases with high morbidity and mortality would tend to have high priority. The sine qua non for support is that there be competent individuals in centers with adequate facilities to carry on the project. It is also important that the research project does not duplicate other research underway. Other things being equal, preference should be given to those programs which are peculiarly significant for Latin America or to those which involve international cooperation. Finally, even if several of the above conditions are not fulfilled, the Committee felt that a project might be considered if its support will have a favorable effect on the research potential of the country."

The limiting factors in implementing the program endeavors are research resources, skilled manpower, and institutional resources and drive. While there are several outstanding research centers and programs in Middle and South America, the important health problems under consideration call for a sustained research development effort by the Americas as a whole and by each country concerned, to develop national and international institutional resources to accomplish the ends sought.

Recognizing that successful research enterprise begins with imaginative, trained, skillful individuals who have the equipment with which to work, the Committee emphasized (page 2, last paragraph) that,

> "A long-range policy in scientific development must have as its basis the detection of young scientific talent, its encouragement, and its promotion through fellowships and other means. All efforts should be made to identify the best existing research

> centers in order to strengthen and supplement their research and to encourage them to foster their own programs of study at the post-graduate level. It is essential to arrange for the education of young trainees within the framework of these centers, so that traveling abroad will be necessary only in exceptional cases. The research and training centers should be supported by providing fellowships for students as well as equipment and funds to cover the expenses of the trainees."

It will be noted that the expanded program is concerned with three broad areas of research which bear directly on the health and well-being of the people of the Americas. These are:

1.- Bio-medical research on certain communicable diseases about which current knowledge is inadequate or non-existent, to bring about their control and possible eradication;

2.- Applied and basic research in environmental health having to do especially with sanitation, pure water supply, waste disposal, and industrial health problems; and

3.- Bio-social research dealing with the economics and social anthropology of health and medical care.

From the standpoint of the Organization's current program interests, it is clear that today, and during the entire 60-year history of the Organization, communicable diseases have the highest priority. This will continue to be so, but if these diseases are ever to be brought under control there is only one way to do it and that is by acquiring, through bio-medical research on the agents and vectors of the diseases, the necessary knowledge to deal with them effectively. These health problems are international ones and the Organization is well equipped to provide leadership and to coordinate intercountry efforts to solve them.

The second category of problems concern the influence of the environment on health and disease. They are manifold. The unsanitary and other untoward conditions which prevail in many regions of the Americas are well known. These are problems which call for research on the application of known principles to local conditions which vary widely in the Americas. Toward this end, the Committee recommended (page 9, second paragraph) that each country establish an experimental station associated with a technical institution,

> "where solutions to problems of applied research, adaptation of known principles, and the training of technological personnel could be stimulated..."

These urgent problems can only be solved by the countries themselves but PAHO can be of assistance in providing, upon request, expert consultant services in planning the experimental stations and research programs.

The third broad category concerns the social and economic aspects of health and disease and of medical care. Concerning the social ecological factors the Committee further recommended (page 9, last paragraph)

> "The need for exploring anthropological approaches, human behavior and mechanisms of mass education to accept new ideas and to change existing habit patterns is as important in treating problems associated with the environment as it is in all public health activities, and warrants emphasis in any consideration of applied research."

Recognizing that the gap between what is known about health and disease and what is being applied in practice is large and may be growing, the Committee observed (page 29, last paragraph) that,

> "research in medical care and its economic aspects would help tie up health with the general growth and development of a country, and establish the basis for a general body of doctrines related thereto. This type of research fits in very well with the present timely interest in the rational planning of many aspects of social and economic development in the Hemisphere."

It concluded (page 30, second paragraph) by giving this field of research

> "a very high priority level on par with biological and medical research."

As a matter of urgent necessity, therefore, the Organization will extend its best efforts to assist Member Countries in mounting research activities looking toward closing this dangerous gap. It is clear that such action is vital to the success of National plans for development in the decade ahead under the Charter of Punta del Este.

In this broad and important field, as in the general area of biological and medical research, national and international research resources for pursuing necessary investigations and for training of research workers determine the pace of progress toward the ends sought.

PAHO Policy on Research

The outlines of a research policy for PAHO emerging from the considerations previously discussed are clear. It has evolved over a period of years as the Organization has gained experience in solving problems in the pursuit of its long-term objectives. However, in facing up to its developing and greatly expanded future responsibilities, in large part reflected in the attached documents, it is well to state explicitly the policy which, with the approval of the Conference, will guide the Organization's action program in the Quadrennium ahead.

The research policy of PAHO is to assist the Americas in the development of the necessary research resources for solving the most pressing health problems of the people.

The guiding philosophy of the proposed policy is that poor health and disease involve the complex of functions of the human organism as a biological entity, and inseparably also the interaction of the individual with his social and physical environment. In short, bio-medical research embraces the study of all the biological and environmental factors which if out of balance and uncontrolled may cause ill health, disease, and incapacity of the individual to function as a normal human being.

To develop healthy modern living conditions involves investigation of how a community, be it rural or urban, lives --an analysis of its systems of communication and cultural institutions and patterns, and the physical environment within which its health services function. From these basic research data, practical plans can be developed involving not merely needed medical care services, but also the necessary involvement of the people themselves in all aspects of preventive medicine and disease control in creating a healthy, sanitary environment at home, at work, and at play.

As was stated at the outset of this report, the expanded research program, as it is being developed, will be related to the distinctive needs and opportunities for research existing within the Member Countries. It will emphasize research projects requiring coordinated effort by more than one country and research activities that will stimulate a wider application of existing and new knowledge to the special problems of each country. Research which will solve operational problems of programs themselves will be undertaken including especially research that will assist the Americas in implementing health components of national development plans. Besides the growing resources of the Americas, PAHO will draw upon the diversified experience of the World Health Organization. The research activities of both Organizations will be fully coordinated, bearing in mind the opportunities and special needs and requirements of the Americas.

Implementation of the Policy

In implementing the research policy, subject to the approval of the Conference, assistance will be made available to the Organization's Governments, upon request, to assess the status of their research resources and to promote their development for the solution of national health problems. The assistance will take the form of expert consultant services for organizing research activities and training programs in existing educational and research institutions, and also, for helping to organize new institutions as needed. Such assistance will embrace consideration, on a high-priority basis, of the economic and financial aspects of health services and medical care in national development planning, a heretofore neglected field of basic research.

Many countries of the Americas share similar health problems and when two or more of them seek to pool scarce resources in an international research center to achieve mutually desired ends and request the assistance of PAHO in such undertakings, the Organization will respond within its available resources, as it has done in the past, by offering its experience and counsel in inter-American cooperative efforts. Moreover, PAHO will undertake to use its good offices in attracting the interest of fund-granting organizations, providing that the countries concerned furnish the basic minimum facilities and personnel required for such partnership efforts.

Recognizing that the establishment of an international research center takes time and realizing that many of the research projects of the expanded program presented herewith should be undertaken with the least possible delay, the Organization will undertake to coordinate the planning of cooperative research efforts of the countries concerned. It will also endeavor to be of assistance in securing the necessary support funds.

Furthermore, in the future as in the past, the Organization will seek by all available means to expedite communication among research workers and public health officials, as well as among educational and research institutions. It will continue to sponsor research conferences, media of communication, and fellowships, and institute a program of research traineeships and in other ways expedite the exchange of information and skills in developing the health-sciences community of the Americas.

In furtherance of these ends, the Office of Research Coordination will develop and maintain an up-to-date roster of the health-sciences research institutions and personnel of the Americas, based on national inventories and assessments.

As the policy unfolds in action, an annual review and appraisal will be made and referred to the Advisory Committee on Medical Research for its critical review and recommendations. Annual reports will be made to the Directing Council and to the Organization's Governments.

The entire program of research development as well as the policy will be subject to review at the next Pan American Sanitary Conference in 1966.

Financial Arrangements

The Organization's program of research to date has been maintained and expanded with a relatively small investment by the Governments sufficient to support a small corps of experts, individuals who for the most part cover several fields.

The investment has yielded great dividends because the quality of work has attracted the interest of other scientists and of fund-granting agencies.

Upwards of one million dollars is contributed annually in the form of research grants from the USPHS National Institutes of Health and from private foundations and other sources for projects at research centers and at Headquarters.

Even with an anticipated one-year extension of the present NIH grant for planning and coordination activity it will become necessary, as the program gathers momentum, for the Organization to fund the costs of the continued function of this office in the amount of $100,000 in 1964, $125,000 in 1965, and $150,000 in 1966.

The program itself which is reflected in the attached Report will be funded project by project as granting agencies become convinced of their merit and of their importance to the health of the Americas.

CONCLUSION

The Americas are on the move and the Organization's role in the vast international and national efforts to raise the standard of living of the people and create a healthier life for all is an exceedingly important one. To discharge its responsibilities to the Governments during a period of revolutionary advances in science, bio-medical research must expand in many directions if the Organization is to continue to merit the same confidence of the international community of the Americas which it has enjoyed for the past sixty years, as a result of the services rendered to combat disease and prolong productive life.

Annexes: I, II, and III.

XIII MEETING
DIRECTING COUNCIL OF THE PAHO

XIII MEETING
REGIONAL COMMITTEE OF THE WHO FOR THE AMERICAS

RESOLUTION XXXVIII

PLANNING FOR THE RESEARCH PROGRAM OF THE PAN AMERICAN HEALTH ORGANIZATION

THE DIRECTING COUNCIL,

Having examined the report of the Director on planning for the research program of the Pan American Health Organization (Documents CD13/15 and CE43/16), and the steps already being taken for the expansion of research in the Region; and

Considering that such expansion of research will be of benefit to the health and medical programs throughout the Americas,

RESOLVES:

1. To approve the plan and policies proposed by the Director of the Bureau in Document CE43/16 in connection with the research program of the Pan American Health Organization.

2. To request the Director to take the necessary action to further intensify the research activities of PAHO for the benefit of the countries of the Region.

(Approved at the sixteenth plenary session, 13 October 1961).

XIII MEETING
DIRECTING COUNCIL OF THE PAHO

XIII MEETING
REGIONAL COMMITTEE OF THE WHO FOR THE AMERICAS

Statement of Arrangements between the Pan American Health Organization (PAHO) and the United States Public Health Service (USPHS) for Research

The general objective of this statement is the establishment of an understanding between the USPHS and PAHO which will aid the organizations in administering their research activities more effectively in countries of the Americas by:

(a) Outlining ways in which the activities of the USPHS and PAHO relating to research in the Americas, particularly outside the United States, may be made more effective through appropriate collaboration.

(b) Stating the general lines of development of PAHO research activities.

(c) Stating the principles under which NIH research grants might be made directly to responsible investigators in the Americas.

1. Staff Collaboration

The informal staff activities characterizing USPHS-PAHO relationships in research will continue. The two organizations will continue to exchange information on plans and actions relevant to their research activities in the Americas.

PAHO is prepared, upon request, to consider provision of advice to the USPHS on support of research in the Americas, and the USPHS is prepared, upon request, to consider aid to PAHO in developing PAHO's research program.

2. Development of PAHO Research Activities

PAHO is prepared to offer more extensive aid to the development of medical and health research in the Americas through such activities as:

(a) Provision of moderate financial support to research projects and programs.

(b) Conduct of research by the staff of PAHO.

(c) Provision of central professional advice and logistical support for research programs requiring coordinated work by scientists in more than one country.

(d) Aid in the development of scientists, scientific communication, and other activities required in connection with research.

3. USPHS Relationship to Developing PAHO Research Activities

The USPHS is willing, upon request, to consider such forms of aid to the development of PAHO research activities as:

(a) Technical advice on research design.

(b) Provision of research grants to investigators who may wish to participate in research programs coordinated by PAHO.

(c) Provision of research support directly to PAHO for research conducted by PAHO staff, or for central professional services or logistical aid provided by PAHO as part of coordinated research programs. USPHS will not make research grants to PAHO from which PAHO will in turn make grants to investigators.

The terms, conditions, and procedures for aid by USPHS to PAHO will be worked out in the light of the circumstances surrounding specific activities.

Communication of the Surgeon General of the United States Public Health Service

8 November 1960

Abraham Horwitz, M.D.
Director
Pan American Sanitary Bureau
1501 New Hampshire Avenue, N.W.
Washington 6, D. C.

Dear Dr. Horwitz:

I am pleased to approve the "Statement of Arrangements between the Pan American Health Organization and the United States Public Health

Service for Research" appended to your letter of October 20. This arrangement, I am sure, will contribute to the development of useful research through the Americas.

Sincerely yours,

(signed)
L.E. Burney
Surgeon General

Pan American Health Organization

World Health Organization

XVI Pan American Sanitary Conference

XIV Regional Committee Meeting

Minneapolis, Minnesota, U.S.A.
August-September 1962

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3 August 1962
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RESEARCH PROGRAM

PAHO

Advisory Committee on Medical Research

Report of the First Meeting

1962

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

PAHO ADVISORY COMMITTEE ON MEDICAL RESEARCH

REPORT OF THE FIRST MEETING

1962

Document RES 1/19
Original: English

3 August 1962

PAN AMERICAN HEALTH ORGANIZATION
Pan American Sanitary Bureau, Regional Office of the
WORLD HEALTH ORGANIZATION
Washington, D. C.

PAHO ADVISORY COMMITTEE ON MEDICAL RESEARCH

1962

TABLE OF CONTENTS

ORIGINAL: ENGLISH

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PAN AMERICAN HEALTH ORGANIZATION

Washington 6, D.C.

Pan American Health Organization

ADVISORY COMMITTEE ON MEDICAL RESEARCH

First Meeting

School of Foreign Service
Georgetown University
Multilingual Room
Washington, D.C.

18-22 June 1962

AGENDA

1. Opening Statement - Dr. Abraham Horwitz, Director, PASB

   Welcome by Dr. Walter C. Hess, Associate Dean, School of Medicine, Georgetown University

2. Election of Chairman, Vice-Chairman and Rapporteurs

3. Introductory Remarks - Dr. Raymond B. Allen

4. Background Information on Past and Current PAHO Research Activities - Dr. Mauricio Martins da Silva (Document RES 1/8)

5. WHO Research Program - Dr. Erwin Kohn (WHO Document MHO/AD/66.61)

6. International Research Activities of the National Institutes of Health, USPHS - Dr. Martin M. Cummings (Document RES 1/10)

7. Needs in Research Training and Medical Education in Latin America - Dr. Ramón Villareal (Document RES 1/4)

8. Research in Environmental Health in Latin America - Mr. Harold R. Shipman and Professor Earnest Boyce (Document RES 1/1)

9. Research Needs in Dental Public Health in Latin America - Dr. Mario M. Chaves (Document RES 1/5)

10. Toward a Research Policy in Maternal and Child Health in Latin America - Dr. Alfred Yankauer (Document RES 1/7)

11. A Nutrition Research Program in Latin America - Drs. J. M. Bengoa, Donald M. Watkin and John B. Stanbury (Document RES 1/6)

12. Report of the Advisory Group on Research in Chagas Disease - Drs. Alfredo N. Bica and Theodor Von Brand (Document RES 1/15)

13. Malaria Research Needs and Opportunities in Latin America - Dr. John Austin Kerr (Document RES 1/2)

14. Research Needs in Schistosomiasis in the Americas - Dr. Willard H. Wright (Document RES 1/12)

15. Leprosy Research in Latin America - Drs. James A. Doull and John H. Hanks (Document RES 1/11)

16. Research Needs in Plague in the Americas - Dr. Karl F. Meyer (Document RES 1/13)

17. Research and Research Needs in Arthropod-Borne Virus Diseases in Latin America - Dr. Antonio Vilches (Document RES 1/9)

18. Zoonoses Problems and Research Needs in Latin America - Dr. James H. Steele (Document RES 1/16)

19. Radiation as Applied to Medical and Public Health Research - Drs. Irvin M. Lourie and Frederick Stohlman, Jr. (Document RES 1/14)

20. Research Needs on the Economics of Health and Medical Care in Latin America - Dr. A. Peter Ruderman; presented by Mrs. Agnes W. Brewster (Document RES 1/3)

21. Research Needs in Medical Care in Latin America - Dr. R. García Valenzuela (Document RES 1/17)

22. Committee Recommendations

23. Closure of the Meeting.

INTRODUCTION

Dr. Abraham Horwitz, Director of the Pan American Sanitary Bureau, stated in his introductory remarks at the First Meeting of the PAHO Advisory Committee on Medical Research that the Organization "has decided to undertake the task of building up a long-range medical research program in the Americas, one of a truly international nature..." and that the Committee had been created in order to "review the existing and proposed research program and make appropriate suggestions," and to "recommend the basis of a long-term research policy for present and future projects, to be approved by the Governing Bodies of the Pan American Health Organization."

From 18 - 22 June 1962, the Committee examined the reviews of the research fields proposed by the Director with the advice of consultants, and its general comments and suggestions make up the body of the present document. In addition, it formulated the following thoughts on research policy:

The Committee understood that it was to deal with research, and with certain related areas such as training and education. It would not deal with the application of existing knowledge even when, as is often the case, the gap between knowledge and application is great. This should be the concern of other bodies.

The Committee did not accept the common distinction between "fundamental" and "applied" science. It felt that all genuine good quality research is fundamental if it contributes to the more complete understanding of the multi-faceted aspects of complex problems. This is particularly so when deal-

ing with man, who is the central object of its concern.

Fundamental science is not distinguished by the use of mathematical, physical, or chemical methods per se, but rather by the relevance of the research to an intellectually and practically satisfactory solution of the problem at hand.

The immediate purpose of supporting research in Latin America is to solve problems related to health in a manner which will promote human welfare. To this end, general areas of research were examined, and a preliminary attempt was made to establish priorities. The long range goal is to promote the upgrading of the community in its most human aspects through the cultivation of science. Indeed, science, if understood properly as a form of culture, is a means of eventually providing the whole community with an objective awareness of the proper context of man; it gives a holistic view of the universe, in keeping with man's intellectual nature; it will eventually provide a basis for mutual understanding; and it is in any case a proper basis on which to build education. Regardless of the individual programs which are undertaken by PAHO, and regardless of the practical results which are obtained - which cannot be predicted because of the essential gamble involved in all research - the objective of upgrading the community will be attained if the men put in charge of these programs are carefully selected for their scientific and human qualities.

A long-range policy in scientific development must have as its basis the detection of young scientific talent, its encouragement, and its promotion through fellowships and other means. All efforts should be made to identify the best existing research centers in order to strengthen and supplement their research and to encourage them to foster their own programs of study at the post-graduate level. It is essential to arrange for the education of young

trainees within the framework of these centers, so that travelling abroad will be necessary only in exceptional cases. The research and teaching centers should be supported by providing fellowships for students as well as equipment and funds to cover the expenses of the trainees.

It is obvious that the research will have to be planned and priorities established. "Genuine planning is an attempt, not arbitrarily to displace reality, but to clarify it and grasp firmly all the elements necessary, to bring the geographic and economic facts in harmony with human purposes."* To the extent that research is a collective enterprise, requiring the contribution of public funds, it has to be planned in a general way. But it must be remembered that research is in the last instance an essentially individual undertaking, subject to all the fluctuations, hesitancies and indeed anxieties of the unknown, and that extreme regimentation and rigidity must be avoided if happy and fruitful results are to be expected.

The basis for the establishment of priorities are several. The research project must be relevant to the field of health and it must somehow promise dividends in terms of new and significant knowledge and of increased human welfare. It is rarely possible to obtain an accurate idea of the economic importance of the problem to be studied, because of lack of data in this area. Since this important criterion could so rarely be used, research on diseases with high morbidity and mortality would tend to have a high priority. The sine qua non for support is that there be competent individuals in centers with adequate facilities to carry on the project. It is also important that the research project does not duplicate other research underway. Other things

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being equal, preference should be given to those programs which are peculiarly [illegible] America or to those which involve international cooperation. Finally, even if several of the above conditions are not fulfilled, the Committee felt that a project might be considered if its support will have a favorable effect on the research potential of the country.

PAST AND PRESENT RESEARCH ACTIVITIES OF PAHO AND WHO

The Committee considered statements of the past and present activities in research of PAHO and WHO and of the several national programs, official and voluntary. The Committee recognized that the volume and effectiveness of research performed under the PAHO and WHO programs were considerably greater than generally realized even before specifically designated research programs had been adopted.

Since the adoption of research as a policy by WHO, however, radical changes had taken place which required a fresh orientation of policy on programs to be supported. Furthermore, the expanded programs of international assistance for research by other organizations, especially the NIH, demanded the most careful scrutiny to ensure that unnecessary duplication was avoided.

The Committee considered that PAHO has the same responsibility for problems facing the Americas that WHO has on a world basis - to foster research which is the life-blood of progress. It welcomed the proposals presented to its first meeting, and its comments in the body of the report were made in full consciousness of the need for coordination of the activities of the two organizations in the sphere of research.

RESEARCH TRAINING IN THE MEDICAL AND HEALTH SCIENCES

The Committee noted that the problems of medical education had been considered by another Committee convened by PAHO and that a program in this field had been formulated. The immediate problem of training medical practitioners, which was made evident from the figures in Document RES 1/4,* should in no way interfere with the imperative necessity of stimulating and developing research activities in the medical schools, which should be carried out pari passu with the formation of physicians to give medical care to the public. Research is inseparable from teaching.

It was recognized that many factors of a socio-economic nature affect the quality and quantity of research productivity everywhere. In spite of some adverse factors, however, good research has been and continues to be done in Latin America, and it is highly desirable that it be encouraged through all possible means. In addition to the results obtained from practical applications of research findings, research serves most useful purposes by helping to stabilize the staff, increasing the degree of excellence of the institutions, and providing the best means towards their long range upgrading.

The Committee recognized that in some Latin American countries a primary deficiency in developing the research potential is the relative lack of opportunity for stable careers in research. Unless these are available with suitable salaries and research opportunities, it will not be easy to attract the best men into research, since they would have no difficulty in achieving a succesful career in almost any other area they choose. As a pre-

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*"Needs in Research Training and Medical Education in Latin America" prepared for this Advisory Committee meeting.

liminary to attaining such stability, the Committee strongly recommended that each country carry out, by means of the establishment of a National Research Council, or by some other means, a radical study of the programs in the health and related sciences, so as to identify where research activities should and could be stimulated and career appointments be made to advantage. It was recommended that PAHO support these studies by offering the services of consultants.

It was the strong belief of this Committee that the single most important handicap to the advance of research in the medical and other health sciences in Latin America lies in the shortage of trained specialists at all levels. For this reason, any program to develop research in Latin America must have as its fundamental and most important objective a training program to improve and increase the current potential of trained manpower in the research field. A solution to this problem will be of the greatest value in contributing to the advance of research in all fields of medicine as well as in the related fields of public and environmental health, dental health, veterinary medicine and others. It was recommended that PAHO give the highest priority to exploring means of support for a program of graduate education and specialist training for research in health sciences, including provision for the continued full-time support of the trainees in research careers. While the Committee recognized that at the present time it is not feasible to designate a specific order of magnitude for the program, it must be conceived on a bold scale and must include provision for long term support, if it is to have the impact on the research potential of the hemisphere which the Committee envisages.

An important part of the work of the National Research Councils

should be to seek for opportunities for research and research training in places which are at present not being used for the purpose. An example of this are the social security hospitals which can readily be brought into affiliation with universities and, as a result, not only ensure better medical care in the hospitals, through the availability of the best consultants and the pick of the medical graduates, but also provide almost unlimited opportunities for research on the major disease problems of the country. The essential factor in this proposal is the affiliation of these hospitals with the research and teaching potential of universities. A logical outcome of this would be the creation of additional research posts at very little additional cost.

In order to encourage research in general in the medical schools, funds should be made available for worthwhile programs undertaken by competent individuals, account being taken of this Committee's recommendations for the individual broad subjects examined in this report. The development of graduate training centers, both in the universities and in special institutes outside of universities, and associated with them, should be strongly encouraged. Full-time positions in research and teaching are highly desirable, particularly in the basic sciences. The possibility of training biologists, chemists and physicists to serve as investigators and teachers in the medical schools should deserve more consideration. In this connection, the Committee emphasized that modern research demands the participation of highly trained scientists in a wide variety of disciplines of the physical and biological sciences, medical training alone often being insufficient. Finally research in the methodology of medical teaching is important and should be supported.

ENVIRONMENTAL HEALTH

The Committee wished to emphasize that the threats to health posed by the environment are local, being influenced by geographic and demographic factors. Furthermore they change rapidly in character, because of changes in technology and because of population movements. Hence, it could be anticipated that the existing knowledge of environmental health would not be sufficient to solve the problems in Latin America, because this knowledge was developed for the conditions prevailing in Western Europe and North America. Indeed it is known that certain kinds of knowledge which apply to certain parts of Europe do not apply to certain parts of North America. For example, the toxic components of air pollution in London, Paris or Berlin are totally different in chemical constitution from the air pollutants characteristic of the Los Angeles or Arizona type of smog.

In view of this high degree of local specificity of environmental hazards, and of the rapidity with which these hazards will change as Latin America becomes increasingly industrialized, the only solution is to create in each region a research center devoted to the study of the special environmental problems of the region. Needless to say, the very complexity of the problems involved demands the participation, and therefore the training, of scientists with various kinds of skill.

Granted the existence of problems peculiar to each region, the fact remains nevertheless that there exists a number of other problems of sanitation which are common to all regions of the world and concerning which there is available a large body of systematic knowledge.

In developing economical solutions for these well known and identi-

fiable problems of environmental sanitation, it would be advisable to provide in each country sanitary engineering experimental institutes where existing technological knowledge could be adapted to meet local needs. While this type of institute might not have as its primary purpose the conduct of research as defined in the terms of reference of this Committee, its functional purpose would serve important environmental health needs.

The Committee concurred with the views set forth in the Consultant's report that these experimental stations should be developed in each country where solutions to problems of applied research, adaptation of known principles, and the training of technological personnel could be stimulated and that such stations should be associated with technical institutions offering technological programs.

Problems which involve more basic research and which are peculiar to Latin American conditions exist and could be expected to develop in such areas as industrial wastes, industrial hygiene, garbage and refuse disposal, air pollution, water, sewage, and food technology.

The Committee noted that the report on environmental health placed emphasis on applied rather than basic research and that some priorities of such research might well follow those established by the PAHO/WHO program priorities. This is to say that applied research might logically begin on such programs as water and sewerage.

The need for exploring anthropological approaches, human behavior, and mechanisms of mass education to accept new ideas and to change existing habit patterns is as important in treating problems associated with the environment as it is in all public health activities, and warrants emphasis in any consideration of applied research. The Committee strongly recommended

that support be given to studies of this nature (See also Maternal and Child Health below).

Although the Committee considered it highly desirable that the training centers proposed in Document RES 1/1* be established by the countries concerned assisted by the Organization, it was felt that provision should be made under the research budget for support of research training of future research workers and of the faculty of these institutes on problems which would certainly arise, even though they might not yet have been clearly defined. This would help to attract faculty of the quality desired. The Committee believed that the nature of the research which might well be undertaken in these centers should be the subject of further study by the Organization and a report on this would be welcomed at the next meeting of the Committee.

The Committee agreed that the health aspects of housing demands the attention of the Organization and that collaboration with the Inter-American Housing and Planning Center should be developed.

The Committee emphasized that, while the provision of pure water and sewage disposal is the most urgent environmental need, studies of other means of transmission of intestinal diseases and their control should not be neglected.

In the special area of occupational health the information provided to the Committee related mainly to one country, Chile, because of the establishment in Santiago of the Inter-American Institute of Occupational Health financed by the U.N. Special Fund, the Chilean government and the University of Chile. Most of the problems mentioned apply as well to other Latin American countries. The Committee observed that it would appreciate receiving more

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*"Report of the Consultant on Environmental Health" prepared for this Advisory Committee meeting.

information on industrial health problems in other countries at its next session.

DENTAL HEALTH

The Committee noted that, out of 17 dental schools which were surveyed (none from Argentina), 10 had no research whatever; in 4, only isolated individuals did research; 1 had a definite research program but no individual funds assigned to it; and only 2 had definite programs with individual funds. This is not an unusual pattern in many parts of the world. The Committee took note, however, that in Argentina there is a long and active tradition of good quality research in dental problems, particularly fluorosis, caries prevention, nutrition, and pathology as related to dental health. Training of research workers in this field and stimulation of a research attitude seemed to the Committee to be the primary need in most places. It appeared that this could not be accomplished on a short-term basis, but support of selected worthwhile research programs in competent hands, where such can be found, might be one way of catalyzing the process.

Within dental health research, it would seem that the following priorities should be considered:

a. Training of research workers

b. Epidemiologic research (see Document RES 1/5)*

c. Research on preventive methods

d. Research designed to increase the efficiency of coverage of dental service programs.

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*"Research Needs in Dental Public Health in Latin America" prepared for this Advisory Committee meeting.

MATERNAL AND CHILD HEALTH

The Committee expressed its general agreement with the stimulating views set forth in Document RES 1/7*. The subject was given a high priority.

However the opinion was expressed that it should not be too readily assumed that increased growth, as indicated by the rate of increase of height and weight in children, is necessarily synonymous with improved health. It was agreed that growth measured in these terms might be a valuable indicator where gastro-intestinal infections and malnutrition are rife, as in many of the Latin American countries, but current knowledge does not justify extrapolation to areas such as the United States where such conditions are relatively rare. The biggest babies are not necessarily the best babies.

The proposals submitted were classified under three main headings:

a. Studies of mortality, morbidity and growth as indices of improvement in the health status of populations The Committee considered that these are essential parts of the evaluation of any attempt to improve health, with the proviso mentioned above regarding the interpretation of growth as an index of health.

b. Studies of methods of accelerating cultural changes favorable to health The Committee strongly urged that such studies be developed, pointing out that their applicability would extend far beyond the field of Maternal and Child Health. The Committee expressed the

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*"Toward a Research Policy in Maternal and Child Health in Latin America" prepared for this Advisory Committee meeting.

view that it would welcome more specific proposals for research on this subject at its next meeting and recommended that the Organization seek appropriate advice from sociologists, anthropologists, psychologists, educators, and others. The Committee pointed out the similarity of this need to that expressed in the section on environmental health.

c. Comparative studies of health services The Committee felt that this is a much needed area of research which has been too often neglected. The application of epidemiological techniques to the study of the functioning and effectiveness of health services has not only been shown to be practical but might be the only way in which an objective evaluation of the real value of services, which are often both empirical and costly, could be made. This type of research also has a much wider field of application than in maternal and child health alone.

The last two items might perhaps be better classified as research in public health practice.

The Committee expressed its concern over the possibly serious effects of the changing pattern of breast-feeding in many areas of Latin America, and strongly recommended studies of this problem.

NUTRITION

The Committee congratulated the consultants upon the high quality of

their report. Because of this, and because there was general agreement with the proposals, few comments were necessary. It was recommended that, in the general PAHO program, research related to nutritional problems should receive the highest priority. Because of the great importance of these studies and the limitation of available funds, however, a tentative list of priorities within the nutrition field was established as follows:

a. Malnutrition in infants and young children with special emphasis on the effects of protein and/or calorie deficiency on patterns of growth and development
b. Anemias
c. Endemic goiter
d. Nutrition and infection.

At this time, the Committee did not wish to establish priorities for specific individual research projects as set forth in the Consultants' report, leaving such a decision to the Organization, if and when funds become available. The Committee wished to emphasize again the need to avoid duplication of research already being undertaken or planned under the WHO program.

CHAGAS' DISEASE

The distinction and the size of the group of consultants constituting the Advisory Group on Research in Chagas' Disease gave great authority to Document RES 1/15*. The widespread occurrence of Chagas' disease throughout

*"Report of the Advisory Group on Research in Chagas' Disease" prepared for this Advisory Committee meeting.

Latin America, its exclusive distribution in this continent, its discovery and early classical description by a South American worker, its economic and social importance, and the many areas of ignorance of the factors involved, make research in this field one of the highest priorities in the mind of the Committee. To this might be added the legitimately proprietary feeling which Latin American workers derive from the almost exclusively continental contributions to knowledge of the subject.

The Committee refered to the consultants' document for a list of priorities and for their justification as follows:

a. Perfection and standardization of diagnostic procedures, primarily because of their importance in evaluating the magnitude of the problem

b. A broad survey designed to evaluate the true extent and magnitude of the problem

c. Ecology of vectors with a view to more radical control

d. Chemotherapy, since to date no therapeutic agent has been found to be really effective against this protozoosis

e. Prophylaxis, mainly envisaging:
   - perfection of methods of applying insecticides, chiefly designed to discover more economical techniques
   - discovery of active substances to combat T. cruzi in blood in vitro

f. Basic research on correct identification of trypanosomes similar to T. cruzi and on the nutrition, metabolism, and immunological behavior of this parasite.

To the above list of priorities the Committee wished to add research on the pathogenesis of the disease, which was implied in the body of the document but not stated explicitly.

The Committee wished particularly to insist on the following:

a. The establishment of centers responsible for producing and controlling antigens for laboratory diagnosis as a means of furthering research

b. The promotion of centers to maintain strains of trypanosomes under known conditions and facilitating their exchange, also for the purpose of furthering research

c. Specifically supporting the centers of excellence already engaged in research on the various aspects of the disease.

The Committee wished to emphasize, apropos of Chagas' disease, a view which could be applied to almost any of the pathological processes considered - that an awareness of the immense range and broad aspects of the problem should be cultivated by workers in this field. A broad front of attack should be maintained to encourage the many and diverse views of the problem - all of them complementary, none of them more "basic" or "fundamental" than the others. Whereas "molecular" or "biochemical and biophysical" considerations should certainly be encouraged, they should not necessarily be thought of as constituting more profound or important contributions than those dealing with original clinical or epidemiological observations or than those which consider the more complex social, anthropological, or behavioristic aspects of the field.

MALARIA

The central problem for research in malaria seemed to be that of insecticide resistance in the mosquito vectors. This might be due to ecological characteristics of the insect which make for a reduced exposure to the insecticide as it is routinely employed; or it might be due to the acquisition of resistance in the mosquito through mutation of certain biochemical traits.

In the first instance, study of the ecological habits of the vector was indicated, such as was widespread in the pre-DDT era. Research on new malaria control measures, in addition to field studies, should be actively pursued.

A study of the biochemical and genetic mechanisms of resistance was indicated, but it was pointed out that this type of work is at present competently being carried out on a large scale under the WHO research program. Certain aspects of this type of fundamental research might provide, however, an interesting challenge for Latin American workers with talent for basic research and a desire to apply it to questions related to public health problems.

Other suggestions for research might be found in the list prepared by the WHO Scientific Group on Malaria Research that met in Geneva on 23 - 27 November 1959 (Document MHO/PA/6.60). The Committee emphasized that the PAHO research program should be considered within the wider framework of the WHO malaria research program.

SCHISTOSOMIASIS

Schistosomiasis is a disease resulting from the intimate contact

between man and the river. It requires for its maintenance a rather complex chain of interdependent biological events, the rupture of any one of which would lead to its suppression. Its incidence is basically limited to three countries in Latin America and to a few islands, and its spread is conditioned by the presence of the intermediate host and the human migrations and settlements in certain valleys. It provides numerous areas for research, both with potential practical applications and with possibilities for research training and stimulation at all levels of fundamental knowledge. It is therefore an excellent subject for research support.

It might be added that schistosomiasis is possibly the only helminthiasis which is on the increase, and that its economic implications are enormous, if the data from the Philippines (where it is said to cause $6.6 million/year loss, more than malaria) could be extrapolated to other areas of the world. Even though much work on the physiology and biochemistry of the worm has been performed, especially by E. Bueding and his group, much remains to be done. A satisfactory and effective chemotherapeutic agent has not been found, nor has a good molluscicide. There is no clear-cut way of judging whether a given infection is active or not, but it is generally agreed that subjects with a better state of nutrition fare better clinically and possibly "resist" the infection to a greater degree.

Bearing in mind the above facts, and based upon the excellent and complete review presented by the consultants, it would appear that the highest priority for research should be given to this disease, at least in those countries where it is prevalent. The priorities for research areas within this field are as follows:

Research on the Molluscan Intermediate Hosts

a. The preparation of a guide for the neotropical planorbids for use by public health workers involved in survey work and control programs of schistosomiasis in the Americas

b. Distribution of intermediate hosts and potential intermediate hosts with special reference to Brazil

c. Additional studies on the biology and chemistry of the aquatic environment to determine the factors conducive to snail harborage

d. Further evaluation of the role of Australorbis tenagophilus in transmission of the disease

e. The genetic and physiologic constitution of various strains of molluscan intermediate hosts in relation to their susceptibility to schistosome infection.

Research on the Control of the Molluscan Intermediate Hosts

a. Intensive effort to develop more efficient and cheaper molluscicides

b. New formulations of known effective molluscicides with synergists, spreading or emulsifying agents or other physical and chemical mechanisms to provide for more effective distribution and to promote residual activity

c. Biochemical and physiological studies to determine the mode of action of molluscicides

d. Research on more reliable methods for the automatic dispensing of molluscicides

e. Development of effective tests for the detection of low dilutions of molluscicides.

Research on the Parasite

a. Development of *in vitro* axenic cultures of *Schistosoma mansoni* to determine basic physiological and biochemical patterns, knowledge which would be of value in the development of new drugs aimed at destroying the parasite or inhibiting the egg laying capacity of the female

b. The significance of lower animal reservoirs in the transmission of the disease and their possible influence on control schemes.

Research Relating to the Human Host

a. Development of more effective and safer drugs without appreciable side effects for treatment of human schistosomiasis

b. Further studies on the mode of action of schistosomicidal drugs

c. Additional studies on the fluorescent antibody technique for the diagnosis of schistosomiasis and evaluation of its usefulness in epidemiological surveys

d. Studies on immune mechanisms in the human host

e. Carefully controlled group studies in a highly endemic area in

which control measures are not operative to determine the effect of fortified diets on the symptomatology of the disease and the egg output of the female worms

f. Group studies to establish clinical gradient standards for schistosomiasis in the America to serve as a base line for determining the economic impact of the disease on the individual and the community.

It might be noted in passing that the greatest care should be exercised in modifying the milieu where the intermediate host lives. The effect of poisonous substances on the ecology of the streams and the possible consequences of the removal of the snail should be carefully assessed before applying the findings of research in these directions.

LEPROSY RESEARCH IN LATIN AMERICA

The presentation of the documentation left no doubt that there is an urgent need to encourage research on this enormous subject because of its economic and public health importance, the persisting ignorance of many of the essential features of the disease, and the distressing but evident fact that it is exceedingly difficult to attract research workers into this field. It was pointed out that for decades leprosy had, as it were, "inherited" the advances made in the study of tuberculosis, but that relatively little had been done in research on leprosy in its own right. This situation was clearly wrong and, further, with the enormous reduction in human tuberculosis throughout the world there is a real danger that even this indirect contribution to

the understanding of leprosy will decrease. Past research on leprosy has been directed mainly to the clinical field and far too little to the laboratory and epidemiological aspects of the disease. There appears to be a grave deficiency of laboratory workers at the present time.

Throughout its considerations the Committee had been most careful to examine the possibility that the research proposed might duplicate research being undertaken elsewhere. However in this field this does not arise, owing to the very small number of competent scientists working on the subject. The Committee therefore recommended that support of research on leprosy by the Organization be determined largely by the known competence of the few investigators studying the disease rather than by detailed examination of specific projects. In this way the investigators would be given greater freedom to follow possible clues to advances than if they were supported only for a specific investigation.

A very high priority was given to this subject.

PLAGUE IN THE AMERICAS

The Committee expressed its appreciation for the remarkably complete documentation provided and the excellent presentation. These provided a unique review of the existing situation in the Hemisphere and an outline of research plans for studies in Perú and Venezuela. It was recommended that on completion of the report on plague for other areas in the Americas, the document should be published. In addition, it was indicated in the presentation that there were reports that sylvatic plague might have spread through to the northern part of Bolivia and might invade the rodent population in the Amazon

basin. It was stated that the actual situation was far from clear but if it were confirmed the possible consequences might become serious. Flooding in this area during the rainy season would provide an ideal situation for spread of the infection among wild rodents which would then be likely to transmit it to man either indirectly through domestic rodents or directly by invasion of villages. It was proposed that verification of these reports by a mobile international team comprising a mammalogist, an entomologist and an ecologist should be undertaken. If they should be confirmed, a plague organization on a regional basis should be set up with the aim of stimulating research, improving reporting, encouraging early recognition of the disease and providing prompt treatment. It was further recommended that investigations should be undertaken on the best rodenticides and insecticides to use in order to prevent familial aggregations of cases so frequently observed in Perú and to a lesser extent in Venezuela.

The Committee believed that the ecological and epidemiological studies outlined in Document RES 1/13* are sound, and should be supported subject to the availability of funds. However, the highest priority should be given to the problem of the definition of the real situation in norther Bolivia. The Committee believed that early steps should be taken to do this, and that the team should then study the situation in the other countries with a view to identifying the best area for further research.

The Committee also stressed the need for increased awareness on the part of physicians of the possibility of plague as a clinical diagnosis in all countries with sylvatic foci. This is particularly important in view of the

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*"Plague in the Americas" prepared for this Advisory Committee meeting.

great reduction in mortality following early treatment. It recommended that PAHO ensure that, in relevant areas, ministries of health, medical societies, hospitals and medical schools are aware of the importance of this fact.

ARTHROPOD-BORNE VIRUS DISEASES IN LATIN AMERICA

The Committee expressed its appreciation for the excellent report provided by the Secretariat and Consultants. It was in full agreement that research is urgently needed in this field, even though it is clear that at the present time the toll in human morbidity caused by these infections is not known. It is believed that this would prove to be considerably higher than is generally thought. However apart from the specific results of research on this subject, the Committee felt that this is one of the most valuable areas for the development of research competence, and certainly one of the best for demonstrating the importance of the ecological approach to medical research. The Committee wished to stress here what could with equal justification have been stressed in almost any other section of this report, that the "orthodox" division of research into basic and applied is most misleading. No one aspect is more basic than another. All are complementary aspects of the approach to the study of life and those factors, including disease, which imperil it. This comprehensive view of research, referred to as the ecological approach, demands that consideration should be given to the relationship of the total organism under study to its total environment, the "total" organism including the biochemical, immunological, and other processes by which it lives, and the "total" environment comprising the biological, physical, and behavioral influences with which it must compete and to which it must adapt

if it is to survive.

The arthropod-borne virus diseases are especially good examples of this, since not only man, but also insect vectors and animal hosts, are involved in their ecology. Man, whose interests are axiomatically the major concern of the Committee, is the least important of the three if one hopes to understand how to prevent human disease induced by these viruses. The investigation must start with the ecology of the virus, its vectors and its natural animal reservoirs. It was partly for this reason that the Committee recommended a high priority for the program proposed.

The Committee was aware that a world-wide program of research on this subject was being developed by the World Health Organization and that the Rockefeller Foundation was participating closely in this through its international virus research program. The Committee was pleased to note that the PAHO program was being conceived in full cognizance of the WHO program. It supported the proposal for a reference center in Latin America as an integral part of the world network of centers being developed by WHO.

All the proposals for research were considered excellent and worthy of support, subject to the availability of funds. However there is a unique opportunity to which the highest priority should be given. This arises from the proposed movement of large populations into the Amazon basin. Past experience elsewhere, such as the high focal incidence of Russian spring-summer encephalitis among settlers opening up new areas in Siberia, and recently the epidemic of Mayaro fever in Japanese settlers in Uruma, Bolivia, stresses the urgent need for ecological studies before such population movements are made. Furthermore man's own interference with the environment of the settled area profoundly disturbs its ecology and hence the prevailing disease pattern. This applies to all types of disease including those which are arthropod-

borne. The study of this matter was considered so urgent and so difficult that the Committee recommended convening a special advisory group to design and supervise these studies. The group should include experts with a thorough understanding of ecology.

The Committee noted that this was the first proposal for research in the field of virus diseases. It agreed with the selection but, as its next session, would welcome proposals for research on respiratory virus diseases which are suspected to contribute largely to mortality and morbidity in Latin America.

ZOONOSES: PROBLEMS AND RESEARCH NEEDS IN LATIN AMERICA

The documentation and the presentation to the Committee on this subject provided a comprehensive review of this most important field. The Committee noted that stress was placed upon the weakness that results from the "fragmentation" of medical and related sciences into sections that are actually part of a whole but are treated as if they were separate. The Committee recognized that in many countries of the world including some Latin American countries the veterinary profession is not given its deserved recognition and is also seriously underpaid.

Where this exists, it is the direct result of the failure of governments to appreciate the enormous contribution that veterinarians could make in the economic and hygienic field in all countries, and particularly in those countries in which stock raising is important. In Argentina, for example, the situation with respect to foot-and-mouth disease is threatening. The Committee noted with satisfaction the measures being taken to deal with this

problem. The prevention of livestock losses that is possible through the employment of well-trained veterinarians equipped with modern techniques, results in savings many times greater than the cost of supporting the veterinary service. It was urged that the attention of the governments of member states be drawn to this fact and to the urgent need for further research, especially in foot-and-mouth disease.

The Committee strongly supported research on this subject, not only because of its economic importance but also because animal populations, both domestic and wild, play a major role in the ecology of many human diseases.

The areas in which research should be concentrated include the following:

a. Training of future leaders in research and program planning

b. Collection of data - especially on the socio-economic impact of these diseases - which might convince governments of the economic advantages of supporting veterinary programs and the veterinary profession

c. Public health application of the known facts about zoonoses

d. Fellowships.

Three further areas were, however, singled out for special emphasis. The first is the need for the provision of standard antigens and sera which could be used in surveys of the distribution of a number of zoonoses both in animals and man.

The second is the development of a system whereby the potency of various veterinary vaccines could be assured by regular testing. The Committee

wished to emphasize most strongly that with all biological products, no matter how experienced the producer, regular testing is essential, and that the failure of individual batches to pass the test carries no scientific stigma. It urged that, not only in this field but also in the field of human vaccines, fullest advantage should be taken of the testing services offered by PAHO.

The third proposal is concerned with the establishment in the Pan American Zoonoses Center in Argentina of a reference serum bank - similar to the WHO World Reference Serum Bank at Yale University - in which collections of animal and human sera would be developed. The Committee agreed that this would be an invaluable augmentation of the WHO program.

RADIATION

Ionizing radiation could be looked at both as an object of study, with reference to its effects on living systems, and as a tool for research in many fields. With regard to the first concept, it would seem that, within the framework and philosophy of this Committee, the proposed research in the document under consideration should have a low priority. Thus, for example, the number of inhabitants in the high background monazite areas of Brazil is too small, the background too inconstant, and the variables too many to make the study worthwhile.

With regard to the use of radiation as a tool for research, on the other hand, it would seem that there are many promising areas in the field of tropical health. A judgment as to priorities in these different areas would seem to depend upon the importance of such areas and their relevance to the objectives of PAHO. Thus, for example, the study of iron absorption

and loss through various routes, being related to nutritional problems, would be given the highest priority. Similarly, the use of ionizing radiation to modify the sexual physiology and the biotic potential of certain vectors, especially the reduviid bugs, would fall in an area of very high priority. The study of hydatid cysts by means of external scanning of the liver following injection of an appropriate isotope would certainly have a high priority.

The value of radioisotope technology as a stimulant to the development of scientific endeavor and the need for supporting already functioning competent groups could also provide a basis for a high priority choice.

An effort to spread knowledge of these useful techniques by means of properly conducted courses should certainly be continued and deserves support.

HEALTH ECONOMICS AND MEDICAL CARE

The economic aspects of health and medical care are poorly understood because of lack of research in this area. It is probable that, with better administration, 20 to 30 per cent more patients could be taken care of in available hospital beds, and hence in the long run the answer to the shortage of beds is not necessarily to build more hospitals, but to perform fundamental research into the how's and why's of such a situation.

In addition, research in medical care and its economic aspects would help tie up health with the general growth and development of a country, and establish the basis for a general body of doctrines related thereto. This type of research fits in very well with the present timely interest in the rational planning of many aspects of social and economic development in the Hemisphere.

Throughout its deliberations, the Committee noted the lack of data which would permit it to evaluate the economic impact of the various studies proposed in other fields, and thus to base the priorities on a surer footing. This, among other considerations, made the Committee keenly aware of the importance of the field of research described in Documents 1/3 and 1/17*.

For all of these reasons, and because of the immediate and long range returns to be expected from this type of research, the Committee did not hesitate to place it at a very high priority level on par with biological and medical research.

CONCLUSION

The Committee was informed of the steps which were to be taken to implement the program. These included the presentation of the report to the XVI Pan American Sanitary Conference for its consideration in August 1962. Programs selected according to the guide-lines on priority given by the Committee would then be prepared in a form suitable for submission to appropriate fund-granting agencies. Clearly in the eyes of the Committee adequate funding of this program is vital.

In this connection the Committee wished to urge that because of the essential importance of research for the more rapid development of the countries of Latin America, serious consideration should be given by the Governing Bodies of the Organization for the support of research in its regular budget.

*"Research Needs on the Economics of Health and Medical Care in Latin America" (RES 1/3) and "Research Needs in Medical Care in Latin America" (RES 1/17) prepared for this Advisory Committee meeting.

The Committee wished to congratulate the Director, the Secretariat, the Staff, and the many experts involved, for the very high standards of scientific excellence attained at this meeting. It wished to re-emphasize the need for continuing at the same high level the plans for the development of the program and recommended that the necessary budgetary provisions be made for this purpose. The Committee noted a request from the Secretariat for suggestions and advice on appropriate research subjects, to be supported by the Organization, for consideration at the next meeting of the Committee, tentatively scheduled for 17 - 21 June 1963.

Part II

SUMMARY OF REPORTS

FOR THE

FIRST MEETING OF THE

PAHO ADVISORY COMMITTEE ON MEDICAL RESEARCH

BACKGROUND INFORMATION ON PAST AND CURRENT PAHO RESEARCH ACTIVITIES*

Research is not a new activity for the Pan American Health Organization. In one form or another it has been carried on for many years. Under the aegis of PAHO, major research programs have been conducted at the Institute of Nutrition of Central America and Panama (INCAP) in Guatemala, the Pan American Foot-and-Mouth Disease Center (PANAFTOSA) in Brazil, the Pan American Zoonoses Center (CEPANZO) in Argentina, and by the technical branches of the Organization.

I. Institute of Nutrition of Central America and Panama

The first research endeavor at INCAP was to conduct a series of nutrition surveys of representative groups of the population in Central America and Panama. Food composition tables were prepared by means of which the consumption of locally available foodstuffs could be expressed in terms of nutrients. The information obtained on the prevalent nutritional problems in the region revealed that the most evident or serious ones were endemic goiter, protein deficiency, riboflavin deficiency and, in some areas, Vitamin A deficiency.

In the case of endemic goiter, the solution seemed relatively simple since previous experience had shown that the iodization of salt was an effective method of control. Nevertheless it was found that the unrefined crude salt commonly used in Central America and Panama could not be iodized in a stable form with potassium iodide. Investigation of other possible sources of iodine showed that potassium iodate provided a stable product.

*From document RES 1/8 compiled by the Office of Research Coordination, PASB.

The problem of protein deficiency was much more difficult, owing to the fact that availability of foodstuffs that were suitable sources of protein was limited. Studies of methods for increasing the production of foodstuffs of animal origin were initiated with the cooperation of regional agricultural organizations. These studies were directed toward finding locally produced products that could be used for feed or forage, or for preparing low-priced concentrates that could be used to supplement the feeding of livestock. Concurrently INCAP began to investigate the possibility of improving the content and quality of proteins in the basic foods of vegetable origin by the use of selected varieties of seed and improved methods of cultivation.

Studies were also begun in experimental animals and in children on the most effective way to add essential amino acids to the cereal proteins most commonly consumed in the area which are deficient in certain amino acids. It was believed that such investigations would provide a better knowledge of the biological value of those proteins and of the possibility of supplementing them with other natural foods or eventually, if it were shown to be practical, with synthetic amino acids. It was also believed that the studies would provide basic information on the relation between protein requirements and the biological value of the proteins.

INCAP also concentrated attention on the characteristics of severe protein malnutrition in children of pre-school age - the group of the population most severely affected. These studies were considered to be indispensable to the subsequent study of the best methods of treatment and prevention. The goal was to devise a food that could be prepared from locally available raw materials at a sufficiently low price to be within the reach of low-income groups. The preparation of vegetable mixtures that would

permit a more rational use of protein concentrates in human feeding (such as cotton-seed flour) offered the best solution.

Long years of research on this problem led the Institute to recomment the commercial production and distribution of vegetable mixture INCAP No. 9, known as INCAPARINA.

Work on the epidemiological factors responsible for prevalent nutritional problems began with studies of the causes of death in children and anthropometric studies of their growth and development. These studies revealed that severe cases of protein and/or calorie malnutrition indicated a much more serious problem affecting the great majority of the population of the area, in less evident form, especially in the early years of life.

The nutrition studies at INCAP also include research in social anthropology. It is hoped that they will assist in the development of more effective techniques of health education as related to nutrition.

Infections and parasitic processes, especially infant diarrheas, were found by investigators at INCAP to be very important factors in the etiopathogenesis of undernutrition. It is hoped that these studies, which are still in progress, will furnish sufficient information to enable the scanty resources available in these countries to be used in the most economical and rational manner possible.

In the diagnosis of malnutrition, INCAP is searching for simple biochemical methods to evaluate the nutritional status of the population, with special attention to protein malnutrition, that can be easily applied in field work.

Among its research plans for the immediate future, INCAP intends to continue the expansion of its epidemiological research which aims to clarify the role of the several factors (the agent, the host organism, and the

environment) that are responsible for nutritional problems. The research on the effects of malnutrition will focus on those cases in the general population in which malnutrition is not easily recognizable, rather than on severe cases that require hospitalization. In this field, following the lead of recent studies in Mexico, research was begun on the unfavorable effects that subclinical forms of malnutrition appear to have on the mental development of children.

Most of the research at INCAP has hitherto centered on children. It is hoped, however, shortly to start a systematic study of the characteristics of the different types of malnutrition prevalent in adults, with special attention to pregnant women and nursing mothers.

II. The Pan American Foot-and-Mouth Disease Center

The research program of the Pan American Foot-and-Mouth Disease Center continues to have two practical lines of investigation - improving the techniques of virus isolation and identification, and improving the methods of protecting susceptible animals against foot-and-mouth disease.

Diagnostic Techniques for Virus Isolation and Identification

In the virus isolation and identification activities of the Center, three of the seven distinct immunologic types of the virus of foot-and-mouth disease have to be taken into consideration, and within these types subtypes of different antigenic behavior have been encountered. These subtypes are of considerable practical importance in vaccination against the disease as the immunity produced by a vaccine prepared from one subtype strain may provide poor protection against infection with another subtype. In this work of subtype isolation and identification the Center works in close collaboration with the World Reference Laboratory for Foot-and-Mouth Disease at

Pirbright, England.

In some of the countries of South America affected with foot-and-mouth disease and in Central America, Mexico, Panama, and the United States, which are free of foot-and-mouth disease, there occurs another vesicular disease, vesicular stomatitis, which is clinically indistinguishable from foot-and-mouth disease. Differential diagnosis is therefore of great importance, and this can be done only by means of laboratory examination. The Center has investigated methods for improving the laboratory techniques employed and the test in current use is a combination of the complement fixation test and a host susceptibility test involving the inoculation of unweaned and adult mice.

Methods of Protecting Susceptible Animals

The vaccines in current use in the protection of susceptible animals against foot-and-mouth disease are inactivated virus vaccines. In a number of countries the virus is still obtained by the inoculation of cattle in slaughter-houses prior to their slaughter for meat. There are many obvious objections to this practice.

The Center is investigating the use of hosts other than the domesticated animals and the use of tissue culture systems. The possible use of rabbits was investigated some years ago, but the resulting inactivated virus vaccines did not prove satisfactory. A development of this work was the research on modified live virus vaccines. The first virus culture method to be improved at the Center was the Frenkel method. Another culture method under investigation is the use of monolayers of cattle or pig kidney cells.

Attention is also being paid to improving the classic method of inactivated virus vaccine preparation which consists of the adsorption of the

virus on aluminum hydroxide gel and inactivation with formalin. Other adjuvants and other methods of inactivation, such as exposure to ultraviolet light, are being studied.

The factors involved in the application of these methods to commercial production scale have been studied in order to aid vaccine production laboratories and provide material for the training courses of the Center.

In the control of vaccine production, research has been directed towards the finding of a substitute for cattle in tests of vaccine potency and a protection test using young adult mice has been developed. This test is not yet in routine use.

In the studies on the use of rabbits as a source of virus for the production of inactivated virus vaccine, it was found that passage of the virus in these animals was accompanied by a loss of pathogenicity for cattle. This finding led to the development of a modified live virus vaccine for foot-and-mouth disease, which is presently in the stage of limited field testing.

In addition to the main program, active research is being conducted at the Center especially on tissue culture and on the application of tissue culture techniques to research on foot-and-mouth disease. The use of primary cultures of cattle or pig kidney cells presents a number of difficulties, and attempts are being made to establish cell lines which retain the susceptibility of the cell to the virus. Other studies contemplate the use of tissue culture methods to identify virus subtypes, to select lines of modified virus, and to study fluorescent antibody techniques. The Center maintains active collaboration with research institutions in Brazil and in such countries as Argentina, Venezuela, Great Britain and France.

III. The Pan American Zoonoses Center

At the Pan American Zoonoses Center, research activities have been oriented more toward the animal reservoir than toward the human infection, simply because the human case is usually the end of the infectious chain. It should also be noted that research at the Center is interwoven with its training and service functions. Some of the Center's research projects are conducted entirely in its own laboratories and its Farm Annex, but the majority of projects involve field operations which must be carried out in one or more countries.

Epizootiology and Epidemiology

Many of the Center's research projects have been designed to provide information about the natural history (epidemiology and epizootiology) of a given zoonotic infection. The intent is to define zoonoses problems more clearly and to search out the best points of attack for the development of control measures.

Studies on ovine brucellosis led to the isolation for the first time in the Western Hemisphere of Brucella melitensis and Brucella ovis from naturally-infected sheep. Studies carried out on the transmission of rabies by vampire bats were inconclusive, but did provide new information on the distribution of that bat and on its ecology. Investigation of the occurrence of rabies in South American wildlife other than vampire bats has been initiated on a limited scale. Studies on wildlife reservoirs of hydatidosis are also in progress.

Outbreaks of leptospirosis were studied to determine the extent and distribution of the disease in domestic and wild animals and in human populations. These studies also led to the discovery of Leptospira pomona

infection in a new rodent host, the pampas cavy. The isolation of L. pomona from a cat belonging to the household in which a case of human leptospirosis had been diagnosed led to studies that are in progress on the pathogenesis of the disease in domestic felines.

A series of cases of infant diarrheas in the local children's hospital has been studied to determine the frequency of salmonellosis and its origin.

Information on the occurence of Q fever in man and animals is being obtained in selected populations of seven countries in which the disease has not been recognized or has been studied very little.

The need for additional and more exact information on the natural history of the zoonoses in the Americas is an evident fact. This means increasing the amount of work being carried out on brucellosis, rabies, hydatidosis, leptospirosis and salmonellosis, as well as the organization of studies to help define the epidemiological picture regarding such diseases as tuberculosis of animal origin, taeniasis and cysticercosis and the arthropod-borne (ARBO) virus infections.

Taking the ARBO virus infections as an example, it is believed not only that the Center should develop an active research program, but that it is in an unusually favorable position to carry out highly productive work. The studies might well be focused on migratory birds and their role in the dissemination and in the periodic waves of infection.

Another research endeavor, now in the stage of final planning, involves the establishment at the Center of an inter-American repository of human and animal sera for use in sero-epidemiological studies of the zoonoses*. The imperative need for serum repositories of this type was indicated in the

*A grant request has been submitted to NIH since the PAHO Advisory Committee on Medical Research met in June 1962.

Report of the WHO Study Group on Immunologic and Haematological Surveys (WHO Tech. Report Series 181). The international nature and contacts of the Center place it in an exceptionally strategic position to carry out this type of project so important for future research.

Control Methods

The development or evaluation of methods for the control, prevention, or elimination of zoonoses in the animal reservoir is one of the most important areas of research for the Center. The Center has evaluated the efficacy of the Elberg vaccine against Br. melitensis infection in goats, the Sterne vaccine against anthrax, and the modified live virus rabies vaccine in bat-transmitted bovine rabies. A similar project is in progress to determine the value of Leptospira pomona bacterin against bovine leptospirosis. A product recommended for the immunization of sheep against hydatidosis has been studied in sheep. With the support of a grant from NIH, studies are in progress on various drugs and compounds in the search for a more effective means of treating canine echinococcosis. A new project, started at the beginning of 1962, is concerned with means of reducing fox populations through an artificially induced reduction of the reproduction rate. The first year of the project is supported by a research grant received from the Argentine Government.*

Diagnosis

The improvement and evaluation of diagnostic methods has received rather limited attention at the Center. A project for evaluating the sero-agglutination tests for brucellosis was begun recently. Some work has been carried out on the sensitivity and specificity of different biological tests for human hydatidosis.

*For the second year, a grant application has been submitted to NIH since the PAHO/ACMR meeting in June, 1962.

Human Zoonotic Infection

In the development or evaluation of methods for preventing a given zoonotic infection in persons who may be or have been exposed, two projects are currently in operation. One involves measurement of neutralizing antibodies in persons who have received killed duck-embryo vaccine for protection against rabies, and the other involves the comparative potency testing in animals of liquid and lyophilized phenol-killed rabies vaccine for human use.

IV. Other Research Activities of the Organization

Regional Development of Epidemiological Studies

An Inter-American Investigation of Mortality was started in February 1962. Because of differences in the extent of certification by medical personnel, terminology, nosological viewpoints, lack of diagnostic standards, and methods of certifying the underlying cause of death, mortality statistics for the countries in the Americas are not comparable. To provide the background for epidemiological research, the circumstances of fatal illnesses are being investigated in nine cities of the Americas with a view to obtaining death rates by cause which are as comparable as possible. As a first step in obtaining satisfactory data, information is being collected from the larger cities where medical facilities are readily available and most deaths are certified by physicians.

The nine cities selected for the study are:

Bogotá, Colombia
Cali, Colombia
Caracas, Venezuela
Guatemala City, Guatemala
La Plata, Argentina
Lima, Perú
México City, México
Santiago, Chile
São Paulo, Brazil

Each death is investigated through interviews in the home, hospital and clinic, and with the physician, so as to obtain as complete a record as possible of the fatal illness, the results of laboratory and other examinations, and the autopsy findings. The sample consists of approximately 2,000 deaths per year in 1962 and 1963 among persons between the ages of 15 and 75 years in each city. A standard questionnaire is being used to record the findings in all cities.

For deaths in all cities included in the study, the underlying cause of death will be assigned by medical referees following the same standards, and utilizing the histories of the fatal illnesses. The assignment of the rubric of the International Classification of Diseases will be in accordance with international rules, and comparable mortality statistics by age, sex, and cause will be developed. A manual of procedures for the investigation was issued in March 1962 in both Spanish and English.

The medical referees are now reviewing the first 3000 - 4000 questionnaires so far completed. A repliminary analysis of these questionnaires will be prepared soon. Collection of data will be continued for 2 years with periodic review by the medical referees followed by statistical processing. Analysis will be directed toward increasing the understanding of the distribution of cancer, cardiovascular and other diseases in the Americas. In the two-year period approximately 40,000 deaths will be investigated on which extensive analyses will be carried out in 1964 and 1965.

The results of the study will be of importance for the following:

1. Improvement of the overall planning for research, especially in the fields of cancer and cardiovascular diseases.

2. Stimulation and development of centers for research in schools of medicine and schools of public health

3. Provision of complementary data to other research studies such as the International Atherosclerosis Study, which includes most of the cities referred to above.

Preliminary analyses of these mortality statistics already indicate that there may be striking differences in the distribution of cancer by site in the countries of the Americas. To explore these differences further, a working group on cancer statistics is proposed as a first step for future studies.* Plans for this working group are being made for either late 1962 or early 1963, if funds can be obtained. Accurate data on morbidity and mortality from cancer will provide the basis for specific cancer research programs.

Venereal Disease Research

From 1947 through 1949 under a grant from the USPHS, PASB carried out a research program in venereal disease in Guatemala.

The evaluation of cardiolipin antigen in serologic tests for syphilis was made under tropical and subtropical conditions, with particular reference to the problem of false positivity in malaria. On the basis of these studies the final determination of levels of sensitivity and specificity was made. The procedure studied (the VDRL slide test for syphilis) was then recommended for use by the WHO, thus replacing the multiplicity of tests by a standardized, inexpensive, and easily performed procedure which is by now the most widely used of all serologic tests for syphilis.

In the space of about 4 years evaluation was rapidly accomplished through a cooperative program uniting a US-based laboratory and a research unit established in an area with extensive clinical material, with a range of ecologic conditions varying from tropical to temperate, and encompassed

*A grant request for this purpose has been submitted to NIH since the PAHO/ACMR meeting in June 1962.

in a relatively small and easily travelled area. This was the first time in the history of syphilis serology that definitive evaluation had been so rapidly made.

Onchocerciasis Studies in Guatemala

During 1947-1953, the USPHS-PASB Onchocerciasis Project in Guatemala provided extensive data on the biology and ecology of the Simulium flies which was published in monograph form by the Smithsonian Institution. The information served as the basis for a pilot study of blackfly control which demonstrated the efficacy of larviciding in individual streams but the impracticability to attempt widespread control.

After evaluative studies of treatment by various drugs, one thousand persons in a highly endemic area were given suramin sodium. This brought about an 85 per cent reduction in biopsy-positive individuals which was maintained for a 3-year period.

Live Poliovirus Vaccine Trials

Starting in 1958, the Organization began the first large-scale field trials of attenuated live poliovirus vaccines, in which nearly one and a half million persons have since been vaccinated and which demonstrated the practicability of this new approach to the control of poliomyelitis in Latin America.

The results of these studies were presented, along with others from investigators in many parts of the world, at the First and Second International Conferences on Live Poliovirus Vaccines convened by the Organization in Washington, D.C., in 1959 and 1960. The full proceedings of these two conferences have been issued as PAHO Scientific Publications Nos. 44 and 50.

Malaria

One of the most recent research efforts in malaria has been made by the Epidemiological Study Team which began its field work in a problem area of El Salvador in April 1961. The team made comprehensive malariological studies of man and his dwellings, of his malaria parasites, and of the vector species of anopheline mosquitoes in the area.

Regardless of whether or not they are susceptible to DDT - the insecticide that is used by the malaria eradication service of El Salvador - the local population of Anopheles albimanus has been observed to be in the habit of entering houses, of feeding on man inside the house, and then of leaving the houses, usually without acquiring a lethal dose of insecticide. In addition, this vector tends to bite man more frequently outside of houses than inside during the early hours of the night.

The observations provide an explanation of why the regular six-monthly residual spraying of the houses in the area does not interrupt the transmission of malaria, and show the need for supplementary methods if the transmission of malaria is to be interrupted.

In the organization of an insecticide testing program, two insecticide testing teams were formed, one of which is at work in El Salvador, and the other in Bolivia. These teams have as their aim the determination of the optimal dosage and spraying interval of DDT on various types of wall surfaces. as well as the testing of any new insecticides that may become available. The organo-phosphorus insecticides malathion and Baytex(R) have been evaluated.

The methods other than residual spraying that are available for malaria eradication are mass drug treatment and larviciding. Small-scale pilot studies of both have been conducted in El Salvador. The mass drug

treatment involved the administration of a mixture of chloroquine and primaquine to two groups at intervals of 14 and 28 days respectively. Under the exceptionally favorable conditions existing in the study areas, the results were excellent; plans are being made for the cautious extension of mass drug treatment to additional large areas.

The pilot study of larviciding has been made in El Salvador because of its monsoon climate, with distinct rainy and dry seasons. The study is still in its early stages, and no conclusions are possible as yet.

In the Amazon Valley of Brazil, the PAHO assisted technically and financially in making an evaluation of the very large chloroquinized salt program that had been undertaken by the Brazilian Government with the aid of the International Cooperation Administration. In addition to a survey of the amount of chloroquine in kitchen salt in 26 localities, the presence of malaria parasites in the blood was correlated with the presence of chloroquine in the urine. In four places in which the incidence of falciparum malaria was relatively high, studies were made of the response of the infection to medication with the standard adult does of 1,500 mg. of chloroquine (as base). The results are still being evaluated. One of the by-products of this study was the development of a protocol for the study of cases of suspected chloroquine resistance of P. falciparum. This protocol is ready for distribution to all malaria workers in the Hemisphere. It is hoped that the protocol will be useful in the Americas and elsewhere in the world in identifying falciparum infections that are worthy of the careful study that is required to substantiate true chloroquine resistance.

NEEDS IN RESEARCH TRAINING AND MEDICAL EDUCATION IN LATIN AMERICA*

The Pan American Health Organization has a unique opportunity to promote and assist in the development of international research and research training in the medical and health sciences in Latin America. Research is a central and indispensable function of an educational institution. Among the functions of medical schools is the development of researchers who will expand the horizons of medical science and practice. The shortage of adequately trained professional and auxiliary personnel in Latin America is a deterrent to the fullest realization of its research potential in the field of health.

The medical education programs in the Americas could be greatly strengthened through furthering the development of research in medical schools. Several ways by which this could be accomplished are suggested below.

Strengthening Research Programs

One of the objectives of strengthening research programs is the training of research workers. By providing the proper environment for creative endeavor, research opportunities make it attractive for faculty members to devote their entire professional time to medical school activities.

There is a need for more talented young people to seek scientific careers. This will be accomplished only where the opportunity for scientific inquiry is an integral part of the total educational process. The provision for support of research training at all levels and of stable

*From document RES 1/4 prepared by the Regional Advisor in Medical Education, PASB.

careers in the bio-medical sciences thereafter will serve to strengthen the educational program.

Priority would be given to research in fields of greatest importance for the improvement of health in Latin America. Fields such as nutrition, epidemiology, pathology, and infectious diseases offer excellent opportunities for valuable research in areas with varied socio-economic and cultural characteristics.

Research in Medical Education

The growth in scientific knowledge and the rapid pace of social change, among other factors, are altering many aspects of medical practice. This will require a review of medical education programs in order to formulate them in greater consonance with present and future needs.

Studies are necessary to determine how the student may be better prepared to face the problems he will encounter. In other words, experiments are needed to find out how the medical school can best teach, and how the student may best learn, to harmonize the scientific and technical advances in medicine to the deeper personal needs of the individual and the broader needs of the community. Means must be found to determine how traditional schemes of teaching are going to fit in an environment where changes are occurring in the patterns of disease, in the provision of services, and in the general socio-economic conditions of society.

The profound socio-economic changes occurring in Latin America will necessarily be reflected in important changes in the training of health personnel. The number of physicians that a country or region needs, the doctrine that is to guide the practice of medicine, and hence the direction to be given to medical teaching; the prevailing methods and concepts; the

relative importance to be assigned to the various subjects of the curriculum, and the consequent organization and administration of medical teaching, are all influenced by this particular moment in history. The trend in the Americas is to integrate the activities for the protection, promotion, and restoration of health, as the most efficient approach to the health problems. All of these factors will determine how many physicians need to be trained and the type of training they are to receive.

It is frequently assumed that the higher the ratio of physicians to the number of inhabitants, the better the medical care; but that is not necessarily so, because the use of medical services depends on socio-economic factors. In fact, there is no proof that an increase in the number of physicians to population, beyond a certain point, will lead to a reduction in mortality and morbidity rates or even to better health in a community. The recommended ratio of physicians to population varies according to the prevailing diseases, the organization of the system of medical care, the available number of nurses and auxiliary personnel, and the various socio-economic factors that influence the use of medical services.

It is urgently necessary to determine the number of physicians that each country needs, but patterns from other countries with different cultures, living standards, political and administrative structures, and economies continue to be used despite the fact that they are unlike those of the developing countries of Latin America. Moreover, the quality of the resources should be taken into account, as should the priorities in medical and social problems.

Studies are necessary to determine the medical specialties to be developed in a country in relation to its community needs. Studies of this type have been initiated in Venezuela where through a survey carried out by

the Ministry of Health in 1958 it was determined that there was a great need for specialists such as pathologists and cardiologists, who were essential to the development of the public health programs planned. As a result of those studies, programs for the post-graduate training of pathologists, internists, and other needed specialists were developed.

Studies are needed to determine the standards of performance of hospitals and public health institutions necessary for the establishment of teaching programs. Hospital and public health facilities are increasing in Latin America; in some cases, however, these facilities are not used to their full extent for educational purposes. An example of this are the clinical facilities of the Social Security institutions in various countries, which are seldom used to more than a very limited extent for medical education purposes.

It is necessary for each country to determine the curriculum content best adapted to its own needs in order to meet the prevailing health problems, and to determine its organization and best methods to carry it out. Problems that deserve special study are those related to the integration of university and medical education, with the goal of improving premedical preparation and providing coherent and correlated teaching throughout the medical studies.

Studies on the integration of preventive medicine and public health concepts in general clinical teaching are of special interest to Latin America because of the trends of development of health services in the countries of the Hemisphere. Various schools in Latin America are already working on research projects related to community problems. An example of this is the teaching exercise involving the participation of students in field work to gather data. As part of their medical education program, some

countries such as Colombia, El Salvador, and Mexico have established patterns of rural medical practice for the students. Medical educators in these countries agree that this practice deserves further evaluation and research in order to fulfill its objectives.

RESEARCH IN ENVIRONMENTAL HEALTH IN LATIN AMERICA*

While the basic problems of environmental health are generally the same in every country, the manner of their solution must of necessity reflect the many variations to be found in geography, demography, social patterns, and cultural concepts.

Progress in an environmental health program requires an understanding and appreciation of many factors in addition to the scientific findings upon which environmental health practices are based. The findings of scientific research remain sterile unless they are assimilated so as to modify practice.

It is the objective of all environmental health programs to produce changes in man's physical environment that will protect him from conditions that, without control, might be expected to exert an adverse effect on his physical well-being.

Such a program, to be successful, requires not only a knowledge of the physical environment and the changes that can be brought about by the application of sanitary science and engineering skill, but also the social and economic acceptance of these changes by the people who live in and are a part of the environment.

While it is important in Latin America, as well as elsewhere, that there be adequate support for basic research in the sciences that provide the foundation for environmental health practice, it is also important and perhaps more urgent to support research that will reduce the gap between what is known to be scientifically true and the possible application of this know-

*From document RES 1/1 prepared by the PAHO Consultant in Environmental Health Research, following a field trip to Venezuela, Brazil, Argentina, Chile, Peru, Colombia, Costa Rica and Mexico during March-April, 1962.

ledge in the solution of the many environmental health problems that confront the peoples of Latin America.

General Need for Research and Development: Water Supply, Sewage Disposal, and Industrial Wastes

Engineers with design responsibility for extending urban water supply and sewerage facilities to meet the needs of industrialization and growing populations are in urgent need of reliable design data applicable to the special conditions that exist in Latin America. Data developed through research studies in the United States and in European countries need to be restudied and adapted with variations reflecting differences in climate, construction materials, economic resources, cultural patterns, and technological differences.

The pressure for the construction of permanent facilities for public water supply and sewerage in response to public health needs and economic demand emphasizes the urgency for support of developmental research that will insure reliability of service and economy of construction and operation.

Countries now without urban sewage treatment plants are finding it necessary to plan not only for domestic sewage waste treatment, but also for the treatment of many complex industrial wastes. In almost every country there is an active interest in obtaining design data for oxidation lagoons and in low cost methods of sewage treatment. In general, engineers responsible for the design of sanitary engineering facilities are well aware of the need for research data relating to the local situation under study and, in some instances, steps are being taken to provide the needed laboratory and experiment station facilities. However, there are few laboratories equipped to make stream pollution studies, including the analysis of indus-

trial wastes - services that are essential in any water pollution control program.

Food Technology

The control and abatement of enteric disease will require first the supplying of clean water and the removal of sewage wastes. In addition, it will require new practices on the part of those who produce, market, prepare, and serve food. While the basic principles of food sanitation are essentially the same for all countries, local customs and economic conditions produce a wide variation in food handling practices and, consequently, there is required a greater adaptation of fundamental sanitation principles.

Garbage Disposal

The collection and disposal of the solid wastes of a city is an essential service in the field of environmental health. Need exists for research studies on the administrative organization and the operational costs of this service together with studies of the methods of waste disposal including incineration, sanitary land fill, and possible salvage through composting.

Industrial Hygiene

There is very little information on the amount of time lost by workers in industry from various causes and its economic significance. Without such information it is quite difficult to plan an intelligent preventive program. A need exists for such studies. Other areas of research need include pneumoconioses and manganese poisoning.

Air Pollution

All the environmental aspects of this problem need to be investi-

gated in various areas of Latin America. Research is needed on:

a. Sources and degree of contamination

b. Nature of contaminants

c. Corrosivity of contaminants

In addition, a statistical study should be conducted to determine the prevalence of respiratory conditions (such as chronic bronchitis and emphysema) among urban and rural populations. This will need to be done by age groups, smoking habits, and history of previous pulmonary disease. Functional tests, personal histories, and x-rays of selected groups may be in order.

Industrial Accidents

Industrial accident rates in many Latin American countries are higher than in some highly industrialized nations that have been carrying on preventive campaigns for some time. It would be of value to study the problem of accident-proneness among Latin American workers, the influence of literacy, socio-economic status, alcohol, and other factors. The cost of accidents and the ratio between direct and indirect costs are other important factors in need of evaluation.

Radioactive Fallout

In the light of the recent air-borne nuclear bomb tests it would be of value to determine such factors as:

a. Air-borne contamination

b. Contamination of water supplies (snowfall at high altitude)

c. Contamination of foods (animal, vegetable and marine).

Insect and Rodent Control

In view of the well developed organization existing for the eradication of malaria, it has appeared reasonable to recommend that research and development studies in the field of insect and rodent control be regarded as a logical extension of the malaria program.

Housing

Because of the relationship between housing and health, ministries of health should become actively engaged in the review and control of the public health aspects of housing projects. The Inter-American Housing and Planning Center (CINVA) located in Bogotá, Colombia, and operating under the sponsorship of the Department of Economic and Social Affairs of the Pan American Union, offers excellent facilities and the opportunity for more extensive collaboration with the Pan American Health Organization in the development of research relating to the hygiene of housing.

Education in Sanitary Engineering. Research Facilities

Progress in environmental sanitation in Latin America is dependent on the availability of personnel trained to apply the principles of engineering science to control and change the environmental conditions that have a detrimental or adverse effect on health. Such persons must learn not only the physical sciences that are the foundation of civil engineering practice, but also the principles of biology and chemistry as applied in the design and operation of sanitary public works.

A review of the educational institutions now training sanitary engineers indicates a need in many places for a sanitary engineering science laboratory equipped to provide instruction in the biological and chemical sciences as they are used by the sanitary engineer in his professional work.

At least one sanitary engineering experiment and demonstration station, complete with laboratory facilities, is urgently needed in each country undertaking a program of water resources development, and in some of the larger countries more than one station may be needed.

It would appear desirable that the proposed sanitary engineering experiment stations operate under the joint sponsorship of the different government agencies interested in the research findings. Ministries of public health, public works, independent authorities, and universities maintaining educational programs in civil and sanitary engineering would be expected to have such an interest.

Through a coordination of academic duties and research activities, not only would it be possible to provide full-time employment for members of the sanitary engineering faculties, but the existence of a research facility within a university would do much to stimulate the interest of qualified students in a field that needs both research and design personnel.

It is believed that sanitary engineering research and development centers could do much to facilitate the exchange of research information in the languages of Latin America and that they would provide a liaison among the major research centers of the world. For example, there is a general lack of information with regard to water quantity design requirements, as influenced by variations of climate, degree of fireproofness of housing and other construction, types of industrial usage, and other factors. There is a tendency to adopt the water quantity requirements of other countries without a sufficient evaluation of modifying factors. Such centers would also serve as research-oriented facilities for in-service training programs for personnel in the several specialized fields of environmental health.

NEEDS AND POTENTIALS IN DENTAL PUBLIC HEALTH RESEARCH IN LATIN AMERICA*

Although lacking the spectacular character of poliomyelitis or the drama of cancer, dental diseases represent, nonetheless, a serious health problem. Dental caries and periodontal diseases are almost universal, imposing a severe burden of pain, infection, or discomfort on most of mankind. This health burden is associated with an economic one - the staggering cost of the curative approach.

In countries with a fast-growing population and with professional manpower increasing at a much slower rate, the best hope for a significant attack on the dental health problem lies in the development and extensive use of economically feasible mass preventive methods, and of curative or restorative methods permitting higher productivity. The philosophy of PAHO's dental research program should be essentially pragmatic in nature and pointing directly toward these two aforementioned goals.

I. Suggested Fields in the Dental Research Program

The acceptance of this philosophy permits the delimitation of four basic areas in the dental research program:

Epidemiologic Research

This research would be firstly descriptive, then comparative, and finally, it would try to identify the factors which might explain the differences observed. Areas of exceptionally high or low prevalence of

*From document RES 1/5 prepared by the Regional Advisor in Dental Health, PASB.

dental diseases, not explainable on the basis of present knowledge of disease causation, would be of particular interest. It is quite possible that, in the process of mapping out dental diseases on a regional basis, significant clues would become apparent. Since epidemiological research provides the basic knowledge upon which additional public-health-oriented dental research will rest, it is felt that the initial emphasis of PAHO's dental research program should be placed in this area.

Research on Preventive Methods

This research would be mostly of a developmental nature, having in mind the possibility of a mass approach. It would involve either taking an established fact, such as the caries-preventive action of a daily supplement of fluoride, and searching for alternative vehicles that have a good potential for mass distribution, or submitting new methods to extensive trials on a community basis. In this area would also be included the verification of hypotheses based on suspected dental disease-reducing factors identified in epidemiological studies.

Research on Productivity in Curative or Restorative Dentistry

Research in this area would be oriented toward an increase in work output per dentist-hour, including such approaches as work simplification techniques, time and motion studies, efficient use of chairside assistants, and expansion of responsibilities of dental auxiliaries. This area of research might be called operational research, and would be closely associated with the general area of research in public health methods or practice. It is better conducted in pilot areas associated with schools of public health or with dental units (sections or divisions) in the national health services.

Research on the Distribution of Dental Services

Whereas research described in the previous paragraph would be conducted within the confines of a dental clinic, research on distribution of dental services is essentially of a community type. The aim is to increase the efficiency of coverage of dental programs. This can be accomplished by increases both in the public and private sectors of dental programs. The word "program" is here taken in a broad sense of how a community organizes itself to service its dental needs. The increase in the public sector of the program may be achieved by improvement in the administration, through lost-time studies, application of results of productivity studies to incremental care programs, and other types of administrative studies. The increase in coverage of the private sector of community programs may result again from increased productivity and also from a higher demand as a result of better health education programs. An area common to the public and private sectors is the development of new systems of payment for dental care based on insurance and co-participation principles. Very little has been done in this area in Latin America and there is a good potential for it.

Research in this area needs to rely heavily upon the support of the behavioral and social sciences, especially cultural anthropology, social psychology, sociology, economics and public administration. A great effort is currently being made in many countries on health education programs, and heavy sums of money are being invested in dental care programs with minimum results. Motivation and opinion studies would go a long way towards avoiding the expenditure of unnecessary effort and in directing action and resources to more productive activities. Research in this area is closely related to the general area of research in medical care.

II. Suggested Activities for the Initial Phase of the Dental Research Program

PAHO's participation in research projects will be limited to those of particular interest to public health and preferably involving a number of institutions in different countries. PAHO will try to stimulate, support, and, when needed, coordinate public health-oriented dental research in the Hemisphere. These activities fall clearly into three groups: 1) training of research workers; 2) services to research; and 3) coordination and collaboration in research projects.

Training of Research Workers

The well-trained, scientific-minded, community-oriented, public-health dentist is the cornerstone for such a research program. The dental public health training program that the University of São Paulo started some four years ago in collaboration with PAHO and the Kellogg Foundation provides a good basis for PAHO's research activities in this field.

The average Latin American public health dentist has not received enough training to develop by himself research projects of a more sophisticated nature. There are weaknesses in his knowledge of statistics and of research design. His lack of experience with newer indices, such as the oral hygiene index or the periodontal index, leaves some doubts as to whether uniform dental examination criteria can be used throughout the Americas.

For a long-range dental public health research program, two basic types of training needs should be met gradually. Selected dentists with good potential should be trained at the doctoral level under fellowships given within the framework of this research program. The candidates would be selected on the basis of their vocation, age, high intellectual

capacity and opportunities for stable careers in their country of origin, preferably in dental schools and schools of public health. At the beginning, schools of public health in the United states would be selected for the training. Later in the decade the training of some dentists at this level should be conducted in one of the Latin American schools. For the more immediate needs of research, a larger number of dentists should be trained at the MPH level through short courses specifically oriented toward research needs. A short training course on dental epidemiology and statistics should be offered to the dentists who would be involved in epidemiological research in connection with PAHO's program, to ensure uniformity of criteria in dental surveys and coordinated planning of studies.

Services to Dental Research

To facilitate and support research in the areas previously identified, PAHO should endeavor to provide the following services:

1. Consolidation of existing data
2. Standardization of procedures and criteria for epidemiologic studies
3. Newsletter on current epidemiologic and applied research, such as information on new areas for applied research with indication of possible sources of technical support
4. Bibliographical service and photocopies
5. Support of meetings of investigators working on a particular problem, whenever the need arises

The volume of work in services to research would parallel the growth of the research itself. An important initial step for PAHO in this area would be the establishment of a center, either at PAHO's headquarters,

or in a university, working in close contact with sub-centers established in other countries. They would form a closely knit system for collection and interchange of epidemiological information, each unit having major responsibility for information on a country or group of countries. A special form might be used to summarize survey findings in a uniform fashion. The forms would be reproduced and distributed to each participating center. In diseases with cumulative characteristics like dental caries, selected age groups might be used for reference purposes to facilitate comparative studies.

In a first phase, the work of the center, aided by the sub-centers, would be the development of a standard form or chart where epidemiological dental information could be summarized. The second phase would involve the actual collection of currently available information from published and unpublished dental surveys. The third phase would involve the comparative analysis of available information. Geographical areas deserving further study would be identified and brought to the attention of interested investigators. Lastly, the fourth phase would involve the actual services for epidemiological research conducted by those public health dentists associated with the overall plan developed in the previous phase.

Coordination and Collaboration in Research Projects

The consolidation and summarization of currently available dental epidemiological information will permit a composite picture of dental caries in the Hemisphere and will open up promising avenues for epidemiological investigation. Data from the surveys of the Inter-departmental Committee on Nutrition for National Defense are already available for Perú, Ecuador, Colombia and Chile. A fifth one was conducted in Trinidad in 1961, and two more will be conducted this year. A problem is already apparent from pre-

vious surveys. The prevalence of caries and mild fluorosis in certain areas does not correlate with the amount of fluoride in the water, using the experience in the U.S. as a basis, and points out to either a more intensive physiological action of fluorine or an alternative source of fluorine in the diet. In this respect it might be interesting to study an area in Northeast Brazil where an extremely low caries prevalence has been described. This area is culturally and racially similar to a surrounding area of high caries prevalence. Fluoride in water does not seem to explain the difference because it has been reported that in this region, which incidentally is a drought area, there are communities in the low caries area which consume drinking water brought from the high caries area.

Salt fluoridation is a preventive measure of importance both to developed and developing countries. Officials in several Latin American countries like Brazil, Colombia,* Costa Rica and Paraguay have expressed an interest in participating in PAHO-sponsored field studies on salt fluoridation.

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*A research grant application has been submitted to NIH since the PAHO/ACMR meeting in June, 1962.

TOWARD A RESEARCH POLICY IN MATERNAL AND CHILD HEALTH IN LATIN AMERICA*

Two characteristics distinguish the field of maternal and child health from other areas of health. They are the biological growth of the human organism and the attitude of special concern expressed by society for this segment of its population.

The phenomenon of growth is measurable. It is also extraordinarily sensitive to a number of intrinsic and extrinsic influences. The Americas contain a variety of ethnic groups living under contrasting social, economic and cultural conditions. These differences are reflected in the birth weights of infants, the growth curves of children and the time of onset of adolescence.

On the basis of reported figures, about four to five times as many women die during the maternity cycle and four to five times as many live-born babies fail to survive the fifth year of life in Latin America as in the higher-income countries of the Hemisphere. The excess risk both to mothers and to young children is more than 50 per cent in every country in Latin America. The greatest relative excess risk occurs in late infancy and early childhood. It is known that reported figures understate the magnitude of the problem, particularly that of maternal and early neonatal deaths. The extent of the understatement is not known.

Even less firm data are available on the precise causes of mortality. However, it is certain that hemorrhage, toxemia, and sepsis account for the vast majority of maternal deaths, the first two causes accentuated greatly by

*From document RES 1/7 prepared by the Regional Advisor in Maternal and Child Health, PASB.

nutritional factors (especially iron deficiency) and the latter by provoked abortion and faulty technique of delivery. The bio-physiological causes of excess early childhood mortality stem clearly from the interacting complex of nutritional deficiency (especially of protein) and frequent exposure to heavy doses of common pathogenic organisms causing respiratory and diarrheal disease.

International Collaborative Research

Many basic gaps exist in our knowledge about the phenomena of conception, reproductive wastage, premature birth, congenital anomalies, and normal and retarded physical and mental development. The variety of population groups and diversity of living conditions in the Americas make this area a rich field for the comparative international study of factors influencing these phenomena. The role of PAHO as collaborating channel and coordinator of such efforts is quite obvious and natural.

The need for more effective, cheaper or more easily applicable preventive and curative tools to combat the causes of morbidity and mortality is also a potential field for collaborative study and field trial. Among the areas for research which may be listed are: diarrheal and respiratory diseases, common infectious diseases of childhood, toxemias of pregnancy, and nutrition.

The Contributions of Research

The very existence of widely discrepant death rates indicates that the application of known knowledge is in itself a method of attacking the problem. However, the role of research as a specific effort to obtain operational knowledge which can be applied more rapidly, with less capital, less skill and fewer resources, is of great importance. Furthermore, since the

ordering and organizing priorities of the elements of any attack are not fixed, a continuous appraisal of them including the concept of demonstrations planned to test hypotheses is essential to the attack.

The key to planning is in its choice of priorities and short versus long-term efforts. Given a finite amount of money, must it be invested in each area simultaneously or can the same amount of money be applied to only one of many areas at a time with better results in terms of saving lives? Can these questions be answered by deliberately varying the emphasis of the attack in different communities and assessing the results over a period of time? It is believed that answers to these questions can be obtained through research and that this type of research is one to which the Organization should give very high priority and for which the Organization should assume primary responsibility. A small study of this type has already been undertaken by INCAP in three communities in Guatemala.

The deaths of mothers and young children and the physical growth phenomena of infancy are sensitive indices of a society's development. It is therefore important to point out the role of epidemiologic studies which relate maternal and child health to the social, economic and cultural structure of society. Such studies serve the purpose of arousing the conscience of society by exposing its faults.

Attempts to study methods of modifying man's cultural environment in the interests of health are extraordinarily few in number. A conspicuous example is the work of the Committee on Food Habits of the National Research Council in the United States of America during World War II. It is known that changes in culturally conditioned food choices, defecation practices, and reproduction patterns could, without any change in the economy, the physical environment, or the health service resources, promote the survival

rather than the death of children. What is unknown is how to produce the desired change. Controlled experiments in the field of community organization could seek answers to this unknown. For example, a trend toward total abandonment or early termination of breast feeding is accelerating throughout Latin America, with serious consequence to infants because adequate breast milk substitutes are not available to the mothers. A method of action might be conversion of the grandmother to favor breast feeding by neighborhood-based group work among grandmothers. Success or failure of action would be measurable on various levels: group-work activity, breast feeding incidence and duration, infant growth and infant survival. Comparision of change in experimental and control groups would be possible.

From the standpoint of the Organization's program goal, the focus of health services research may be stated as follows: given a series of known health problems set in specific conditions of life, what is the relationship of the investment of funds in known knowledge (in terms of personnel, supplies, facilities and the organization of all three elements) to the return (in terms of lives saved and disabilities prevented)? Examples of types of hypotheses which can be tested by planned study are:

1. Disease and death among families receiving health services is not randomly distributed but strike some families more frequently and severely than can be accounted for by chance alone.

2. Selection of such vulnerable groups and distributing services (especially preventive and counselling services) proportionately to them will affect the disease and death rates in the population more favorably than distributing services in a direct population ratio.

3. The delivery of preventive and counselling services during or

shortly after an illness episode is more effective than delivering them in health (i.e. at routine intervals).

4. The number of visits a mother is being asked to make for prenatal care of child health supervision can be reduced appreciably without adverse effects.

5. Redistribution of present personnel and services as between domiciliary, clinic and hospital care and the creation and systematic use of intermediary resources such as day-care, convalescent units, and progressive care units in hospitals will improve results.

Methods of Study of Health Service Administration

The best approach to the past is retrospective analyses of deaths, especially those deaths which from available reports are of a "preventable" character, such as those from infection. Such studies have been most successful in the case of maternal deaths in the United States but there is no reason why they should not include the obviously preventable deaths of early childhood within their scope. Information collected by interview of consumer (and giver) of services as soon as possible after a death is necessary in order to supplement what may or may not be available from existing records. The health services given are compared to standards of medical diagnosis and treatment. Preventability of the death is characterized in terms of lack of health service, failure of existing service (poor medical judgement, etc.) or parental neglect, or a combination of factors. The nature of the preventable factors provide the clues to remedy the defect. If they involve errors of medical judgement, they carry a built-in lesson for the physician. Often the organization of such studies can provide clues to community action or information of value to the organization of health services as well.

Studies of the past and present provide useful clues to improving future service, but the really important studies of health service operations must be prospectively designed. In prospective studies, two (or more) groups are compared. One group receives the services in the manner of the past, the other group receives them in an altered manner or from personnel whose knowledge of assignments have been modified. Base-line and terminal measurements of results are calibrated in objective terms such as days of disease, deaths or growth of children. Cost factors are documented for both groups. This approach to services is the same as the concept of clinical trials as applied to a new drug. The hypothesis to be tested might derive from one of the studies of past or present services or might be one of these mentioned previously as seeming logical but needing to be put to the test. In any case the control group represents the standard in this type of study. If services to the experimental group result in fewer lives lost or better growth at the same cost or if they result in equal health at lower cost, such studies provide the patterns for the future reorganization or reorientation of health services.

A third approach to the study of health services is through the consumer. Interviews can seek information on past and present experiences with health services as well as consumer recommendations of use to future planning. In addition, attitudes and practices toward health can be explored and expectations probed so that the content and delivery of services can be guided accordingly. Furthermore, consumer interviews taken at varying periods of time can provide additional measurements of the effect of changing health services.

A Suggested Policy for PAHO

The type of research described needs to be promoted and supported.

The field, zone and central office staff of the Organization can undertake its promotion but are not always able to provide the consultant services necessary to designing and supervision the studies. In some cases personnel to collect the information being assembled in a given study must be trained and paid for their time. It is usually very difficult to draw them from country health service personnel already employed in giving service because of the tremendous service demands. In other cases, however, only a minimum of special training or extra time is required of the service personnel and the principal need is sound study design, instrument preparation and statistical processing.

It is proposed that as a matter of Organization policy a unit for health services or evaluative research be created as a working arm with funds at its disposal. Such a unit would function as follows:

1. It would provide field statistical-social science consultation through short term consultants paid by the Organization in situations where health service research projects have been stimulated by the regular or project staff of the Organization. If this type of consultation can be provided by existing staff, short-term consultants may be unnecessary.

2. It would pay for or provide such items as data collection instruments and statistical processing (coding, tabulation, analysis) and supplies.

3. It would administer grant funds according to a matching formula so as to stimulate the country's involvement in the process of research. Such funds would be used to pay for the supervision and training of data-collecting personnel such as interviewers and to pay the salaries of these personnel during the data collection period.

The staff of such a unit initially might consist of a social scientist with a good statistical background and a sound orientation in health services and practices, and supporting clerical services.

A NUTRITION RESEARCH PROGRAM IN LATIN AMERICA*

It is evident that one of the factors that has brought about an increase in the development of nutrition programs in the Americas is the existence of a large storehouse of knowledge that needs only to be applied. However, much still remains to be learned on the subject.

The PAHO has been engaged in research activities in the field of nutrition for a long time, especially at INCAP, and, to a lesser degree, in collaboration with the Institutes of Nutrition of Ecuador and of Perú. Moreover, WHO Headquarters has given some assistance to the Venezuelan Institute of Scientific Research to study the anemias.

The PAHO Advisory Group on Nutrition, which met in Washington in January, 1962, concluded that a proper orientation of nutrition programs required additional knowledge of the epidemiological aspects of malnutrition (especially of protein-calorie malnutrition in children), hypovitaminosis A, ariboflavinosis and endemic goiter. It is also stated that the effects of malnutrition on physical and mental development had to be ascertained, and that the definition of mortality attributed to malnutrition needed to be improved. The group also pointed out the necessity for making additional studies on high-protein foods, the relationship between nutrition and infectious diseases, the prevalence and causes of the anemias, and the special nutritional needs of nursing mothers.

In addition to these problems, the Group agreed that it was necessary to improve the methodology for the evaluation of the nutritional status and for education in nutrition programs intended for different cultural,

*From document RES 1/6 prepared by the Regional Advisor in Nutrition, PASB, with Consultants from the Massachusetts Institute of Technology and the Massachusetts General Hospital, and staff members of INCAP.

social and economic groups at all ages.

In April, 1962, the PAHO called together a group of consultants to discuss some specific projects of high priority in nutrition research. The following four research areas were given the highest priority:

1. Endemic goiter
2. The etiology and pathogenesis of anemias
3. The effects of nutrition on patterns of growth and psychomotor development in children in Latin America
4. Interrelationships between nutrition and infection

A Research Program in Endemic Goiter (Iodine Metabolism) in Latin America

Endemic goiter is considered to be a public health problem when its prevalence is greater than 10 per cent. In the Americas - excluding the Caribbean Islands - there are areas in all the countries where the prevalence is higher than 10 per cent. Uruguay, where the problem was thought not to exist, is no exception.

It is consensus among investigators at the present time that iodine deficiency is the principal cause of endemic goiter. However, it is apparent that endemic goiter continues to present perplexing problems. It might be profitable to list these at this juncture.

1. More complete information is needed concerning the incidence of goiter in various age groups in many foci throughout Latin America. This information needs to be correlated with the incidence of cretinism, deaf-mutism, and mental and skeletal retardation.

2. Precise comprehensive inventories are needed of the population

structure of isolates where endemic goiter and cretinism are found. This kind of information is required if we are to learn the relationship between endemic cretinism and endemic goiter.

3. More information is needed regarding thyroid function in patients with endemic goiter.

4. The problem of endemic cretinism is in urgent need of detailed study.

5. The relationship between diet and endemic goiter is not yet understood. This problem can only be attacked where field units for metabolic studies can be established.

6. Genetic contributions to the development of endemic goiter need to be explored. Methods are available for testing patients for several well defined types of metabolic blockade which impair thyroid function.

7. An explanation needs to be sought for the anomalous findings of high radioiodine uptake in patients in the interior of Venezuela who do not have goiter.

8. More information is needed on optimal programs for the prophylaxis of endemic goiter.

9. There is a compelling need for information regarding methods for suppressing radioiodide accumulation to low levels in order to prevent iodine uptake by the thyroids of young children at times of I^{131} fallout. Varied programs of suppressive medication need to be explored in this group.

The above list of problems and projects seems formidable, and yet it should be apparent from the remainder of this report that most, if not all, of these can be attacked realistically by competent investigators already in the field with confidence that many, if not most, of these can be answered

within a reasonable period of time. It should be noted that a secondary gain will be the promotion of scientific enterprise in a number of centers in Latin America.

Fortunately, several laboratories exist at the present time near foci of endemic goiter and are staffed by competent and trained people capable of attacking many of these problems providing suitable impetus and support is given. Five or six laboratories in Latin America will be selected for these studies.

Research in Anemias in Latin America

Throughout the Americas the amount of anemia and its several associations with malnutrition, parasitism and infectious diseases are generally underestimated and little understood. Nutrition surveys have provided extensive information on the prevalence of anemia by area and among the various population groups. The same surveys have provided limited information on the morphology of the peripheral red cells in such anemias. The stage is set, therefore, for a more intensive assault on the pathogenesis of anemias in the Americas. Understanding the pathogenesis of particular anemias is an essential prerequisite to the introduction of measures for anemia prevention and control. Three major types of anemia are present in the Americas: (1) hypochromic, microcytic; (2) macrocytic and (3) hereditary. Probable pathogenic factors in type (1) are: a) deficiency of dietary iron; b) excessive loss of iron via skin and bowel; c) parasitism and possibly d) protein deficiency. Probable pathogenic factors in type (2) are folic acid deficiency; B_{12} deficiency and possibly deficiency of ascorbic acid. Probable pathogenic factors in type (3) are the genetic variants in individuals manifesting sickle

cell and Mediterranean anemia. Since it is essential that limited resources be concentrated on specific causal factors of major importance, a precise analysis of pathogenesis must be the first step toward reducing the prevalence of anemias.

Therapeutics will suggest itself naturally when pathogenesis has been determined in specific cases. Therapy must not only assist the individual but must be practical for application to population groups. In consequence, far more is involved than applying a textbook solution to an identified problem. Food supply, dietary custom, environment, economics and hereditary and multiracial backgrounds suggest that practical solutions must be novel and thoroughly investigated in man prior to their introduction as public health measures. Therefore, the second step in reducing the prevalence of anemia must include not only therapeutic trial but also the trial of new, practical and acceptable variations of basic therapy.

The specific aims of the research in the anemias are: (1) to identify the major environmental (including nutritional) and hereditary factors and to quantify the relative importance of these factors in the pathogenesis of anemia; (2) to investigate therapeutic measures suggested by (1) with the objectives of a) confirming by therapeutic trial the pathogenic role of the environmental or hereditary factors and b) seeking practical measures leading to a reduction in the prevalence of anemia. These studies will be carried out in two or three centers of Latin America.

The Effects of Nutrition on Patterns of Growth and Psychomotor Development in Children in Latin America

Anthropometric measurements and patterns of growth and development are considered among the best indexes of the nutritional status of children.

No country in Latin America, however, has accurate and reliable standards, and almost always the nutritionist must use either foreign standards or arbitrary figures.

Since a large proportion of the children living in technically under-developed countries suffer from protein malnutrition at some time during their pre-school years, it is important to have detailed knowledge of the immediate effects and sequelae of various degrees of protein malnutrition. Preliminary results already obtained from cross-sectional studies in the community of Tlaltizapan, México, indicate that retarded psychomotor performance of unknown duration is associated with the degree of malnutrition responsible for the retarded growth and physical development which are almost universal among lower income groups in most Latin American countries, Africa, India, and the Middle and Far East. If studies confirm these findings, i.e., that protein-calorie malnutrition can cause retarded mental, as well as physical development, it would then become even more important to apply emergency measures for the prevention of protein malnutrition in early infancy. It would lend fresh urgency to present world-wide efforts to develop new and inexpensive protein-rich foods and to use more widely those already demonstrated as being practical. Instead of depending on long-term effects of agricultural improvement alone, supplementary feeding programs for infants and pre-school children would receive an even higher priority. Hundreds of thousands of children could thus be rescued from preventable mental damage that could decrease their ability to absorb education and to realize their full potentials of contributing to the progress of their countries.

Anthropometric studies have revealed that in both rural and urban communities of technically underdeveloped areas where malnutrition is prevalent the average measurements of children at birth do not differ from those of

the newborn in more advanced regions. During the first 4 months of life, furthermore, growth rates of babies in those underdeveloped areas are satisfactory; and, if only weight gains are considered, they are equal or even may exceed the patterns established for average North American or European children. After four months, however, the growth rate diminishes progressively, building up a difference from the normal which attains its maximum somewhere between 18 and 24 months. After this age the rate of growth apparently increases and starts to close the gap between the children of underdeveloped areas and their counterparts elsewhere. The magnitude and especially the duration of this better growth, nevertheless, is not sufficient to enable these children to reach normal growth, so that at adolescence malnourished children are lighter and shorter than are children of the same ages in other parts of the world.

Preliminary studies of the mental development of babies in the under-developed countries using the Gesell, Terman-Merrill, and Goodenough tests have shown that they are born with scores higher than the average, but these scores drop rapidly and reach subnormal levels at about 20 - 24 months. The deficit is about 30 per cent at 42 months of age and continues constant throughout school age into adolescence.

The purpose of such studies would be to investigate the physical and psychological development of children belonging to population groups having widely different genetic and cultural backgrounds and also living under different socio-economic and nutritional conditions. To secure a variety of nutritional and genetic conditions, typical communities in Latin American countries would be chosen for this longitudinal study. Initially three or four countries that have professionals especially trained in studies of growth and development would be chosen. The groups to be studied would be

selected from populations with different socio-economic, cultural, and environmental characteristics; and the specific criteria for selection would include the ethnic composition of the group, its degree of urbanization, the type of its economy, and its dietary pattern. Social anthropologists, statisticians and nutrition experts would provide technical assistance in the application of these criteria in determining the groups to be used for the sampling.

Interrelationships Between Nutrition and Infection

Children with a variety of acute and chronic infections are being studied at INCAP by metabolic balance techniques to determine the degree to which additional losses of nitrogen, calcium, vitamin A, ascorbic acid, and other nutrients occur. Children with severe intestinal parasite burdens are similarly studied before and after treatment. Significant adverse effects of yellow fever and smallpox vaccines as examples of very mild viral infections are being found.

Morbidity and mortality from all diseases in children under five years of age are being studied in three rural highland Indian villages of Guatemala by bi-weekly visits to every family and each child is examined periodically to measure growth and maturation and to determine nutritional status. One village serves as a control; and in a second an intensive nutrition education and experimental feeding program is maintaining the children under five in a relatively good nutritional state. In a third village children are treated specifically or symptomatically for every infection and every effort is made to prevent infections by immunizations, latrine construction and other environmental sanitation measures and health education.

The specific aim is to demonstrate the reduction in the severity of infections in children who are well nourished and the improvement in nutritional status of children who are not under severe infectious stress. The experiment, which is in the third year of a planned five year study at a cost of approximately $100,000 per year, is proving successful in achieving the first aim and partially successful in the second. In addition, a great deal of extremely useful data are being obtained on the epidemiology of diarrheal and other infectious diseases in the communities.

It is expected to carry out these studies in three or four areas in Latin America.

REPORT OF THE PAHO ADVISORY GROUP ON RESEARCH IN CHAGAS' DISEASE*

The fundamentals of the present status of knowledge of this disease were summarized in the report of the Study Group on Chagas' Disease which met in Washington, D.C., in March 1960 (WHO Technical Report Series No. 202). This report stressed the seriousness of the health problem posed by Chagas' disease not only because of the extensive area affected with a minimum of 7 million infected individuals but also because pathological processes not previously known to be associated with this disease are being brought to light. Lack of knowledge on basic aspects and on control measures makes the situation even more pressing. Consequently, it is expected that much may be learned from different research approaches including those from the basic sciences.

The Parasite

Characteristics

Research envisaging a precise definition of variations in such biological attributes of the parasite as virulence, parasitic specificity, etc., is indicated to determine whether these characteristics actually have a genetic basis or whether they represent simple variations due to experimental conditions. The following criteria are suggested for such a description:

1. Behavior in vertebrate hosts of different species with emphasis on parasitic specificity, virulence as indicated by parasitemia and mortality, as well as variations in the organotropism and other characteristics

*Met in Rio de Janeiro, Brazil, 4 - 7 June 1962

2. Behavior in invertebrate hosts, particularly with regard to specific variations of sensitivity
3. Proof of cross-protection in laboratory animals
4. Studies on antigenic specificity through agglutination tests following cross-absorption and through specific immunochemical techniques
5. Biochemical characteristics in relation to differences in synthetic capabilities and studies on the various ways in which carbohydrates and other substances are broken down.

A basic condition for the success of studies in this field and many others is the establishment of centers responsible for careful study of a specific number of selected strains and for maintenance of these strains under known conditions for the purposes of supplying investigators.

Culture

To date most methods employed for the culture of T. cruzi have not differed substantially from those used at the beginning of this century. The media are based on whole blood or blood components, occasionally combined with extracts of organs. These conditions make the media difficult to prepare and unsuited for certain types of research where the possibility of contamination of the media in which they are grown should be avoided. In recent years some progress has been made in obtaining simpler media which make it possible to produce large quantities of trypanosomes under more suitable conditions for study.

Continued research along these lines is recommended in view of the many benefits it may provide. The need should also be stressed for studying

culture methods to obtain the bloodstream form and the tissue stages which are present in the vertebrate host.

Nutritional Requirements and Metabolism

As to the nutritional requirements of T. cruzi, the literature shows very little data because the organism has resisted attempts at culture in chemically defined media. Lower trypanosomes, such as Leptomonas oncopelti, Crithidia fasciculata and, more recently, Leishmania tarentolae, have been cultivated in synthetic media and their nutritional requirements determined.

In the case of higher trypanosomes, such as T. cruzi, little-known factors must be involved since it has been demonstrated that they cannot grow in these media. In view of the fundamental nature of information on nutritional needs and its importance in orienting therapeutic research, the Group recommends that continuation of this work be encouraged.

The Group was able to analyze the important progress made in the field of carbohydrate metabolism in trypanosomes. With reference to T. cruzi, a few characteristics of its metabolic processes are known which differentiate it from trypanosomes of anterior evolution. These biochemical data have made it possible to establish a correlation between physiological and morphological data and have assisted in the establishment of phylogenetic relations. Enzymes of the Embden-Meyerhof scheme, and of the Krebs cycle, as well as a terminal oxidase were demonstrated. Very recently the mechanism of succinic acid accumulation was studied and it was demonstrated, with the use of labelled CO_2, that this is actually a partial reversal of the Krebs cycle involving CO_2 fixation. Nevertheless, considerable research is still needed, primarily to investigate certain metabolic by-passes, such as the pentose phosphate

pathway, or to investigate the nature of the terminal oxidase which is inhibited by cyanide but which is uninhibited by CO.

In addition, consideration should be given to studies on the biosynthesis of nucleotides suggesting possible therapeutic uses. Very recently, important studies were carried out on the mechanism of incorporating substances from the medium, demonstrating that, when competing carbohydrates are used, active transport phenomena are involved. Unfortunately, practically nothing is known about the metabolism of proteins and lipids. High concentrations of lipids were found in trypanosomes, including cholesterol and particularly large amounts of phospholipids, but nothing is known concerning their biosynthesis and breakdown.

Immunology

The need was expressed for new diagnostic methods and for defining the degree of specific homogeneity of the parasite and the role of hypersensitivity phenomena in the pathogenesis of the disease. It was acknowledged that these studies are still in rudimentary phase owing to the difficulty in obtaining large quantities of the study material. The following studies are indicated:

1. Antigenic composition of strains, using methods based on gel diffusion and immunoelectrophoresis
2. Antigen fractionation and study of the behavior of such fractions vis-à-vis serum from Chagas' disease patients
3. Detection and identification of possible toxic substances that may be responsible for the lesions in the vertebrate host

4. Mechanism of lysis of crithidial forms of T. cruzi by sera from certain animal species
5. New methods to obtain sera with higher antibody titer than obtained to date.

Although recognizing the limitations in effectiveness and ease of application of active immunization with live or killed organisms the Group recommends that such research be continued.

Diagnostic Methods

The main problems open to investigation in the field of parasitological diagnosis are:

1. To increase the sensitivity and simplify the technique of xenodiagnostic methods
2. To search for more sensitive laboratory animals and evaluate the results of sub-inoculations.

Since the diagnosis of the chronic forms has been based on serological methods, research should be carried out to obtain simpler procedures. This will require:

1. The preparation of more uniform, stable, and purer antigens
2. Based on results obtained with other infections, particularly virus diseases, it is recommended that plate techniques for complement fixation in the diagnosis of Chagas' disease be improved.

Other tests have been described for the immunological diagnosis

of this infection, such as agglutination, conditioned hemolysis, search for incomplete antibodies, hemagglutination reaction, or the use of fluorescent antibodies. Although none of these tests has been shown to be superior to those previously considered, they should be improved upon or new techniques developed.

The need for obtaining comparable results in epidemiological surveys in various endemic areas requires the establishment of regional centers that will be responsible for preparing standard antigens for distribution. These centers would also be responsible for certifying antigens prepared by different labotatories.

The PAHO is requested to furnish technical and financial cooperation for the establishment and operation of these centers.

Physiopathology

Research is needed on the pathogenic mechanism of the chronic form, particularly with respect to the possible role of bouts of parasitemia derived from the infection itself or from superinfections of exogenous origin. Epidemiological longitudinal studies among groups with high rates of T. cruzi infection are recommended.

The best known manifestation of the chronic phase of Chagas' disease is chronic cardiopathy. However, further investigation is needed on:

1. The percentage of chronic cardiopathies ascribed to Chagas' disease in Latin America and the role of other etiological factors unrelated to T. cruzi, that may produce cardiopathy with similar characteristics.

The Group underscores the advisability of geographical pathology studies in Chagas' disease. Since a broad international study on the pathology of atherosclerosis is already underway in the Hemisphere, it is recommended that PAHO explore the possibility of extending the study to include cardiopathy due to Chagas' disease. To this end, it is suggested that the collection of necropsy material include the heart and other organs.

2. The similarity of the cardiopathy due to Chagas' disease, non-specific chronic myocarditis, and the endomyocardial fibrosis described in certain regions of Africa.

In the pathogenesis of the cardiopathy, clinical studies are needed to determine the role of:

a. the parasite as direct physical agent in the inflammatory process
b. substances from the breakdown of the parasite
c. sensitization phenomena either caused by the parasite or resulting from lesions in the cardiac fiber
d. other mechanisms that might be responsible, either wholly or in part, for this cardiopathy.

The study of cardiopathy caused by Chagas' disease should cover not only those individuals who have overt manifestations of the disease, but also and principally asymptomatic cases.

Important evidence indicates that in the areas where Chagas' disease is endemic the digestive as well as the cardiac manifestation may be

evidence of the chronic form of the disease. Consideration is given to the importance of studying:

1. The prevalence of digestive manifestations, either megaoesophagus or megacolon, or manifestations of digestive dysrhythmia, in endemic and non-endemic areas.

   The need was stressed for establishing uniform criteria for the histopathological and physiopathological characteristics of these manifestations. To this end, more objective and more easily performed techniques, such as radioisotopes, should be applied.

2. The possible role of other factors such as viral or nutritional factors as the sole or contributing cause in the genesis of these digestive manifestations

3. Existing data on the experimental production of digestive organomegaly are scant, and consequently it is recommended that these studies be extended, particularly with reference to the role played by T. cruzi in these processes.

In view of the need to extend these studies and to adopt comparable methods, it is recommended that PAHO provide facilities to enable researchers to exchange information through personal contacts, fellowships or travel grants - especially for pathologists - and through specialized training of personnel.

Since the time of Carlos Chagas the existence of nervous and psychic manifestations has been noted in the chronic phase of Chagas' disease. Studies are still lacking to determine the frequency and significance of these

processes. Lesions of the nervous system have been shown in T. cruzi infections. It is recommended that clinical and experimental studies on this aspect of the problem be intensified.

Recent studies have revealed important metabolic and functional changes in the chronic phase of Chagas' disease. These changes are characterized by exaggerated response to certain stimuli, including those of a pharmacological nature and especially cholinergic ones. The results obtained to date indicate that the metabolic studies should be expanded.

Chemotherapy

The problem of specific therapy assumes particular importance in connection with Chagas' disease, considering the chronic nature of this infection and the fact that spontaneous cure has not been observed. Several drugs have been shown to have suppressive action, especially against the blood forms in the acute phase. However, none of these drugs has been demonstrated to effect a permanent cure.

Most of these drugs can be included in the following chemical groups: bisquinaldines, trivalent arsenicals, phenanthridine, methoxi-8-aminoquinolines, nitrofurazones, and purine analogues, especially the ribofuranosilpurines. It was emphasized that the suppressive action of these drugs, although occasionally intense, has only been observed in the acute phase of the infection both in laboratory animals and in humans. This points up the need for research designed to find substances with a more favorable action in this phase and which are also effective in the chronic form. The need for establishing criteria for evaluating the therapeutic action of drugs in ex-

perimental and human Chagas' disease was underscored.

Epidemiology

A better understanding of the factors involved in the epidemiology of Chagas' disease is a vital element in the objective evaluation of its magnitude for the assignment of priorities among health problems in Latin America and as a basis for a control program. While recognizing the medical and health importance of this infection, it must be realized that it is also a zoonosis and as such it possesses inherent characteristics that must be considered.

An evaluation of the elements involved in the epidemiology of this disease requires:

1. Precise knowledge of the areas infested by domestic triatomes, with a determination of the indices of infection by T. cruzi
2. A determination of the prevalence of human infection in these areas by the complement fixation test on representative samples
3. Where human infection has been confirmed, evaluation in samples of different age groups of the severity of the disease as determined by clinical examinations, by electrocardiograms - particularly for individuals over 20 years of age - and, whenever possible, by radiological examinations, especially of the heart and the alimentary tract
4. Notification of acute and chronic cases of this disease
5. The underlying cause of death specified in the death certificates of individuals who have died from various manifestations of Chagas' disease.

Reference was also made to the advisability of undertaking anatomo-pathological studies in the interest of a better understanding of the role of this disease in mortality in different areas. Studies of this type are already being conducted in a limited area, and it is recommended that this survey be extended to other regions.

Available data on the frequency of Chagas' infection among blood donors and confirmed cases of accidental transmission by transfusion call for an evaluation of this problem. This could be done by carrying out serological surveys in blood donors and through a careful followup of patients receiving blood from individuals who are subsequently found to be chronically infected.

The fact that cases of transmission of infection from mother to child are being observed on an increasing scale calls for better evaluation of the importance of transmission through the placenta and through the mother's milk.

The zoonotic nature of Chagas' disease assumes various aspects, with special characteristics that deserve investigation:

1. In the endemic areas with domestic vectors, the dog, the cat, the guinea pig, and, rarely, other domestic animals have been found to be infected. It is suggested that an evaluation be made through xenodiagnosis of the importance of these animals as sources of infection.
2. In other areas where triatomes and non-domestic mammals have been found to be infected by trypanosomes morphologically similar to T. cruzi, it is suggested that a study be made of the conditions of transmission of the infection among these animals.

These parasites should be isolated in both vertebrates and triatomes for identification and study.

3. The vectors and peridomiciliary reservoirs should be carefully investigated in order to assess their role as a link between extra-domiciliary and domiciliary infection.

In areas where T. rangeli has been found, and particularly in others where the natural vectors have been discovered, the use of methods leading to positive identification if this protozoon is recommended, together with more extensive studies permitting a better understanding of its role in human pathology.

Vector

In order to combat more effectively the triatome vectors of Chagas' disease, the intensification of studies on the ecology and physiology of these insects is considered to be of primary importance.

From the physiological viewpoint the following research is necessary:

1. A study of the metabolism of the insect
2. Investigations to obtain a more exact knowledge of the parasite-host relationship and of the factors influencing transmission
3. Studies on the metabolism of insecticides in these triatomes, especially on the determination of the mechanism of action and the possible development of resistance.

In the field of ecology, it is advisable that studies be made not

only on auto-ecology but also on the ecology of triatome colonies, with special emphasis on regional, and possibly local characteristics. In reference to auto-ecology, it is recommended that special attention be given to reproductive activity, metamorphosis, mobility, feeding frequency and feeding preferences and the influence on these aspects of variations in environmental conditions.

With regard to ecology, emphasis should be placed on factors associated with the dynamics of colonies not only with respect to geographic distribution, dispersion and displacements, but also to the limiting factors regulating density, natality, longevity, and mortality of these insects.

In addition to the methods that have been used for such studies, it is recommended that research being carried out using radioactive substances be extended.

Control

Although it recognizes the important role that improvement of rural housing accompanied by better health education could play in the control of Chagas' disease, the Group insists upon the urgency to extend and intensify the use of insecticides because of their more immediate results.

The use of residual insecticides over large areas of Latin America against the triatome vector of T. cruzi has resulted in a very sharp decrease in the population of these insects in dwellings and in a marked drop in the incidence of human infection.

Despite the favorable results obtained by the application of insecticides in millions of dwellings in the poorest regions of Latin America, the Group recommends further studies in the search for better insecticides and

more data on the extent of the surface area to be sprayed, on the optimum insecticide concentration to be used and, especially, on the intervals between insecticide applications.

It is suggested that a study be made of the possibilities of introducing sterile individuals, or carriers of dysgenic factors as a method of vector control.

With regard to rural housing, improved construction introduces a radical change in the ecology of the triatomes and reduces their density. In view of the technical difficulties still presented by the problem of improving rural housing, it is suggested that an effort be made to intensify studies designed either to improve the various housing types already existing or to obtain economical rural housing unfavorable to the proliferation of triatomes.

As to health education, research should be carried out with a view to developing techniques to enlist the population of the endemic areas in the fight against Chagas' disease.

With relation to blood transfusions, the difficulty in excluding donors infected with T. cruzi with any degree of certainty makes it advisable that studies on drugs already demonstrated to be effective against T. cruzi in vitro in the blood (tri-phenylemethanic dyes) be extended, and that new drugs with such action be sought.

The fact that the presence of T. cruzi in mother's milk has already been observed indicates a need for investigations designed to clarify the factors involved in such transmission, to determine its frequency, particularly in the chronic form of the disease, and to institute prophylactic measures.

Coordination of Activities for Research Programs

The Group believes that PAHO could play an important role by:

1. Contributing to the establishment of centers responsible for producing and controlling antigens for laboratory diagnosis
2. Promoting the establishment of centers to maintain strains of trypanosomes under known conditions and facilitating their exchange
3. Standardizing diagnostic techniques
4. Coordinating studies in order to obtain more economical and efficient spraying methods
5. Promoting an exchange of information through the granting of fellowships and the organization of meetings of specialists actively interested in the various aspects of the disease
6. Facilitating the training of research technicians and auxiliary personnel
7. Collecting, analyzing, and disseminating information
8. Stimulating and supporting studies that require coordinated efforts of research workers in various countries
9. Cooperating with different countries by formulating or carrying out research programs through the provision of specialized consultants
10. Contributing to a better knowledge of the mortality from Chagas' disease through coordinated anatomopathological work and by placing greater stress on this disease in case reporting and in death certification

11. Assisting research projects on Chagas' disease with PAHO's own resources or with those obtained from other international organizations.

Priorities

Recognizing that the establishment of an order of priority for the problems to be investigated will depend largely on local conditions regarding the personnel and material available, the Group lists the following fields of study that should be given preference:

1. Improvement and standardization of diagnostic procedures
2. A broad survey designed to evaluate the extent and magnitude of the problem
3. Ecology of vectors
4. Chemotherapy, since to date no effective therapeutic agent exists
5. Prophylaxis, mainly envisaging improvement of methods of applying insecticides and discovery of substances active against T. cruzi in blood in vitro
6. Basic research on the identification of trypanosomes similar to T. cruzi and on their nutrition, metabolism and immunological behavior.

MALARIA RESEARCH NEEDS AND OPPORTUNITIES IN LATIN AMERICA*

The strategy of malaria eradication is simple: to interrupt the transmission of malaria for three years, which is the length of time needed for all the malaria parasites to die out in the human population. The tactic of malaria eradication is also simple: to spray the insides of all the houses in malarious areas twice a year with residual insecticides, such as DDT.

The eradication of malaria was considered to be an operation that was 95 per cent administrative, and only about 5 per cent biological. When the campaign started in the Americas in 1955, it was known that there were areas in which the residual spraying of all the houses twice a year would not interrupt transmission and that some "additional measure" would have to be employed. Because of somewhat overoptimistic estimates of the time and manpower needed to overcome administrative difficulties, insufficient effort was spent on developmental research regarding additional measures. At present there are a number of problem areas in which the malaria is "refractory" to eradication by house spraying alone. In these areas field research to determine how best to solve the problems is under way by the Organization's own personnel, in cooperation with the national malaria eradication services.

Needs in Operational Research

The items of incidental or operational research that follow are those that have come to light in Latin America and merit attention because

*From document RES 1/2, prepared by the Malaria Eradication Branch, PASB.

of their importance there.

1. The epidemiology of refractory malaria, i.e., malaria in problem areas in which adequate residual spraying does not completely interrupt transmission.

2. Ecology of the anopheline vector of malaria in problem areas. This basically is a phase of the preceding item, but is large and complicated enough to merit separate mention and consideration.

3. Evaluation and testing of "additional" eradication methods (i.e. additional to residual spraying) for use in areas with refractory malaria. There are only two accepted methods available for additional use: larviciding and mass drug treatment. Both of these are expensive and difficult to administer; therefore the development of the most efficient means for their application is necessary and urgent.

New and still untried additional measures need to be evaluated under controlled conditions.

4. Chloroquine-resistance of P. falciparum is a phenomenon for which the eradication programs, not only of countries in Latin America, but of the entire world, need to be constantly on the alert. The preliminary screening of suspect cases to eliminate those that are merely chloroquine-tolerant, and to identify those that are worthy of careful study in human volunteers is a detail of operational research.

5. Medicated salt is a procedure that might become an additional method of malaria eradication, where it is possible to make the procedure more efficient and more acceptable to the population.

6. Establishment of criteria for the recognition and precise delimitation of areas of stable malaria, so that major attention could be

devoted to them. If they could be identified it might be possible to reduce very greatly the cost of malaria eradication.

Needs and Opportunities in Basic Research

It is not to be expected that basic research can be conducted by people who are actively engaged in the administration of field operations. These fundamental problems have to be looked into in the more leisurely atmosphere of academic institutions.

Institutions in the Americas in which basic research might be fostered are:

The Institute of Tropical Medicine of the University of São Paulo; the Instituto Nacional de Endemias Rurais in Belo Horizonte, Brazil, and the Gorgas Memorial Laboratory, Panama City, Panama. The Middle America Research Unit has a unique position in relation to Latin America, situated as it is in the Canal Zone. Basic research is going on in the USA in a number of places, including several dependencies of the USPHS, such as the National Institute of Allergy and Infectious Diseases, and the Communicable Disease Center.

Several comprehensive lists of subjects for basic research in all the diverse fields of malariology have been prepared and distributed by WHO. The short list of three items that follows represents known opportunities for research in Latin America rather than eventual needs.

1. The establishment in Latin America of a reference laboratory for studies of human malaria parasites is imperative. It is particularly important that strains of P. falciparum that are suspect of being chloroquine-resistant be carefully studied in human volunteers. It has been suggested

that the facilities in investigators, equipment, and the indispensable "patients" available at the Institute of Tropical Medicine at the Faculty of Medicine, University of São Paulo, would be adequate for such a study.

2. Studies on new formulations for chloroquinized salt might be undertaken at the Instituto Nacional de Endemias Rurais in Belo Horizonte, Brazil.

3. Studies of the simian malaria in Latin America as related to the malaria eradication program are indicated.

SCHISTOSOMIASIS IN THE AMERICAS*

General Background

Schistosomiasis mansoni in the Americas is endemic in some of the Islands of the West Indies and in Venezuela, Surinam, and Brazil. Based on reports of the recent PAHO visiting team (1962), it is estimated that between 4,250,000 and 6,270,000 persons are infected. The prevalence and intensity of infection vary greatly in different countries and in different areas. There has been some recession of the disease in some of the Caribbean Islands, although this does not apply to all. In Guadeloupe and Martinique, the disease has not been reduced appreciably. The same applies to St. Lucia. Transmission no longer occurs in St. Kitts and probably not in Antigua. There has been a marked decline in Puerto Rico in the last 20 years. Schistosomiasis has never been an important health problem in the Dominican Republic but the present foci should be eradicated to prevent any future spread.

Marked progress has been made in control in Venezuela where intensive efforts have been exerted over the past 20 years or more. The situation has not changed materially in Surinam. In Brazil, the disease has actually spread to new areas. This dissemination has been largely associated with the heavy migration southward from the Northeastern States. However, in some areas, control efforts have succeeded in limiting infection.

Australorbis glabratus is the intermediate host throughout the Caribbean, Venezuela and Surinam and is an important host in Brazil. In the latter country, Tropicorbis stramineus and A. tenagophilus are also involved

*From document RES 1/12 prepared by the PAHO Consultants on Schistosomiasis Research.

in transmission. Other species have been found susceptible to infection in the endemic areas and elsewhere but are not known to be involved in transmission. In Brazil, the molluscan intermediate hosts have acquired the ability to withstand prolonged desiccation and thus to some extent maintain the infection over the dry season. In Brazil, the snails have also adapted themselves to extremely varied habitats.

The lack of reporting, the varied clinical manifestations, the low death rate and other factors render difficult any estimation of the economic impact of schistosomiasis. Estimates have been made but such would hardly satisfy the critical economist. One carefully controlled study in the Philippines provided more specific data, which warranted extrapolations as to the economic burden for the country as a whole. It was estimated from the basic data that the total annual loss was $6,632,500, a loss which exceeded that due to malaria.

Control Measures

Methods available for the control of schistosomiasis include the installation of sanitary facilities, control of the molluscan intermediate hosts through the application of molluscicides by engineering procedures and/or by biological methods, attention to lower animal reservoirs of infection in areas in which such definitive hosts are concerned in transmission or potential transmission of infection, chemotherapy, and public health education.

A program for the installation of sanitary facilities should be tied to general health improvement schemes. Populations in many areas are slow to alter age-old habits, and benefits from new installations cannot be

expected to materialize rapidly. In a few instances, sanitary control has failed. The successful application of molluscicides results in a rapid interruption of the transmission of infection. If the chemical is effective also against snail eggs, the cycle of transmission continues to be interrupted until reinvasion of the treated areas. More effective chemicals are needed for snail destruction. Usually molluscicides have to be repeated over a long period of time before control can be achieved. Application is not a simple process and must be correlated with the local ecology of the snail hosts and with the nature of the aquatic environment. Engineering methods are effective for snail control in some situations while biological control has been achieved in localized situations but has not been applied on a large scale. Mass chemotherapy of human carriers has been employed in a number of endemic areas but the net results are open to question. Present drugs lack desired efficacy and have disagreable side effects which discourage patients from completing an entire course of treatment. However, chemotherapy has undoubtedly reduced intensity of infection and complications.

Future Problems

The proposed reclamation of agricultural lands in northeastern Brazil through the extension of existing irrigation systems and the establishment of new systems will increase the possibilities for spread of schistosomiasis in an area in which the disease is already a major health problem. Any plans for the rehabilitation of the area should undoubtedly take into consideration the potentialities for the spread of infection.

In addition to the extension of the disease into previously non-endemic regions, the rapid increase of population since 1940 in Brazil,

Venezuela, Surinam and the Dominican Republic indicates that, at the present growth trend, by the year 2000 there will be nearly a five-fold increase over 1960. With increased migration of workers from congested to sparsely settled areas in each of these countries there is a possibility that the calculated Schistosoma-infected persons will increase accordingly from the 1960 estimates.

Research in Schistosomiasis

Present inability to control schistosomiasis is linked largely with a past dearth of research effort. As a consequence, answers are lacking for many of the vital questions which pertain to control. The following research problems are suggested as being some of the ones which are of most immediate concern and which have a bearing on the public health aspects of the disease.

Research on the Molluscan Intermediate Hosts

a. The preparation of a guide for the neotropical planorbids for use by public health workers involved in survey work and control programs for schistosomiasis in the Americas, as recommended by the PASB/WHO Working Group for the Development of Guidance for Identification of American Planorbidae Involved in Schistosomiasis at its meeting on 6 - 9 November 1961

b. Distribution of intermediate hosts and potential intermediate hosts with special reference to Brazil

c. Additional studies on the biology and chemistry of the aquatic environment to determine the factors conducive to snail harborage

d. Further evaluation of the role of Australorbis tenagophilus in transmission of the disease

e. The genetic and physiologic constitution of various strains of

molluscan intermediate hosts in relation to their susceptibility to schistosome infection.

Research on the Control of the Molluscan Intermediate Hosts

a. Intensive effort to develop more efficient and cheaper molluscicides

b. New formulations of known effective molluscicides with synergists, spreading or emulsifying agents or other physical and chemical mechanisms to provide for more effective distribution and to promote residual activity

c. Biochemical and physiological studies to determine the mode of action of molluscicides

d. Research on more reliable methods for the automatic dispensing of molluscicides

e. Development of effective tests for the detection of low dilutions of molluscicides.

Research on the Parasite

a. Development of *in vitro* axenic cultures of *Schistosoma mansoni* to determine basic physiological and biochemical patterns, knowledge which would be of value in the development of new drugs aimed at destroying the parasite or inhibiting the egg-laying capacity of the female

b. The significance of lower animal reservoirs in the transmission of the disease and their possible influence on control schemes.

Research Relating to the Human Host

a. Development of more effective and safer drugs without appre-

ciable side effects for treatment of human schistosomiasis

b. Further studies on the mode of action of schistosomicidal drugs

c. Additional studies on the fluorescent antibody technique for the diagnosis of schistosomiasis and evaluation of its usefulness in epidemiological surveys

d. Studies on immune mechanisms in the human host

e. Carefully controlled group studies in a highly endemic area in which control measures are not operative to determine the effect of fortified diets on the symptomatology of the disease and the egg output of the female worms

f. Group studies to establish clinical gradient standards for schistosomiasis in the Americas to serve as a base line for determining the economic impact of the disease on the individual and the community

In summary, schistosomiasis is an important public health problem in parts of the Americas, although in a few areas the disease is regressing. Control effort is needed in some of the West Indies islands and in Surinam and Brazil. Venezuela is well along in this respect. It is fortunate that in many of the endemic areas, there are numerous capable investigators who have conducted outstanding research in the field. There is no dearth of talent. Many of these problems are receiving attention in Caracas, Recife and Belo Horizonte as well as in Puerto Rico and elsewhere. What is needed are expanded facilities, additional personnel and more funds both for research and control.

LEPROSY RESEARCH IN LATIN AMERICA

Brazil is said to have more than 150,000 cases; there are more than 22,000 in leprosaria and about 5,000 healthy children of leprosy patients in preventoria. More than 700 physicians in Brazil are engaged in leprosy work, most of them on a part-time basis. In Venezuela, with an estimated total of 15,000 cases and fewer than 1,000 patients in institutions, the annual cost of the leprosy program is about U.S. $2,500,000 or 2.2 per cent of all expenditures for public health and hospitals. Surinam has only 2,500 estimated cases but more than one-fifth of the patients are in leprosaria; the annual cost is about 9 per cent of the total budget for public health and hospitals. Figures for Argentina, Colombia, México, Paraguay, and Perú likewise indicate not only a great humanitarian problem but also a sizeable economic one.

Summary of Present Knowledge

A noncultivated acid-fast bacillus (Mycobacterium leprae) can be demonstrated in a large proportion of cases presenting the clinical syndrome of leprosy. Such a bacillus is rarely found in other diseases or in healthy persons. Leprosy has not been transmitted to any experimental animal, although promising reports have recently been published by several workers.

The mode of transmission is unknown. The present idea is that the bacillus reaches the skin of a susceptible individual by indirect or direct contact with a bacilliferous case, usually lepromatous, and is rubbed or scratched into the skin. The conditions favoring spread are far more effective in warm than in temperate climates.

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*From document RES 1/11 prepared by PAHO Consultants in Leprosy Research, following field trips to Argentina, Brazil, Colombia, México, Perú and Venezuela, during April - May 1962.

Although the lepromatous case is undoubtedly more infectious than the tuberculoid it is possible that the latter type may also be an important source. Tuberculoid cases may discharge many bacilli during periods of reaction and these reactions may be more frequent in some environments than in others. Another point is the potential infectivity of the indeterminate class of cases, a question which is discussed later.

Natural resistance to leprosy is apparently the most important factor which limits prevalence. Increasing frequency of resistance with age is the logical explanation of the rapid fall of the attack rate after the age of 15 years in families in which lepromatous disease is present. This resistance is positively correlated with reactivity to lepromin but this must be only a part of the story because patients with tuberculoid leprosy are usually highly reactive to lepromin.

Drugs of the sulfone group are universally used today in the treatment of leprosy. Controlled studies in lepromatous leprosy have shown that these drugs yield beneficial results but are slow in action. They are bacteriostatic rather than bactericidal; after three years about half the patients are still bacteriologically positive. Relapse is common if treatment is discontinued. Streptomycin and a thiourea (CIBA 1906) are about equal in value to the sulfones, but are much more expensive than the basic sulfone, 4-4' - diaminodiphenyl sulfone (DDS). Other features limiting the value of therapy - especially as a preventive - is that there is usually a long period of latency or slow progression during which the disease is unrecognized but during which the individual may be infectious to his contacts.

It is obvious that there are many lines of research which are scientifically justified and that a choice between them should be determined by the availability of competent scientists rather than by arbitrary

administrative selection. Apparent duplication should be disregarded. Both in England and in the United States, a few investigators are working on transmission of the disease. This does not mean that the rest of the world should sit down and await the results.

Proposals for Specific Research Projects

Single-Country Projects

Four groups of investigators have been encouraged to prepare definite plans for research work and to try first to obtain financial support directly from the National Institutes of Health of the United States Public Health Service. A fifth investigator was encouraged to seek renewal of a current grant. A sixth project on the therapy of leprosy is under way in Venezuela with support from the World Health Organization.

"Direct Cytologic Study of the Skin in Leprosy"

Investigators: Dr. Renê Garrido Neves, Lygia Madeira Cesar de Andrade and Dr. Candido Oliveira da Silva, Instituto de Leprologia, Serviço Nac. da Lepra, Rio de Janeiro, Brazil.

> "With a view to throwing light on the mechanism of resistance to leprosy the types of cutaneous cellular response to natural infection and to the injection of lepromin are to be studied. A direct method of examination will be used, similar to that of modern studies of exfoliated cells in the diagnosis of cancer. Instead of the usual biopsy speciman, scrapings from the corium will provide the materials for study. One interesting possibility is that in patients under treatment with sulfones and whose lepromin tests are negative, microscopic examination of cells scraped from the site of injection of the lepromin may give evidence of a favorable cellular response."

"Cultivation of M. leprae in Human Phagocytes"

Investigators: Dr. Murilo Paca de Azevedo, Instituto de Pesquisas

Leprologicas and Dr. Ednir Antonina Lehmann Wanderley of the same Institute, Dept. de Profilaxis da Lepra, São Paulo, Brazil.

"The purpose of the proposed work is to cultivate the leprosy bacillus in human macrophages obtained from patients and from normal persons, including cells from human histiocytic tumors. The reason for using macrophages is that they are considered to be of the same lineage as the epithelioid cells of the leproma. The patients and normal persons chosen as donors of tissue cells will be lepromin-negative because this is considered to indicate lack of cellular resistance to leprosy."

"Study of Ecological Factors in Leprosy"

Investigators: Drs. Carlos Sisirucá Quintero, Enrique Rasi Bellabene and Jacinto Convit, División de Dermatología Sanitaria, Ministerio de Sanidad y Asistencia Social, Caracas, Venezuela.

"The principal objective of the proposed study is to search for environmental factors associated with the frequency or severity of leprosy in Venezuela. Two principal rural zones in which the disease is endemic, one mountainous in Western Venezuela, the other at a lower level in the Eastern section of the country are to be selected for study. Each zone will be divided into sectors according to known prevalence rates. A complete house-to-house census and sanitary inspection will be made followed by physical examination of all inhabitants. Careful diagnostic studies will be made in every case or suspected case of leprosy. A special investigation will be made of the arthropod population in the search for a possible vector."

"Biochemical and Bacteriological Properties of Mycobacteria Isolated From Leprosy Patients"

A group of investigators of the Sección de Bacteriología, Unidad de Patología, Hospital General, México, D.F., under direction of Dr. Luis J. Bojalil, has been encouraged to send an application to the N.I.H. for support.

"Studies on Chemotherapy of Leprosy"

Investigators: Dr. Jacinto Convit and others, División de Dermatología Sanitaria, Caracas, Venezuela.

This study of drugs initiated by the WHO Leprosy Section at Geneva is still in the planning stages. As a preliminary step the sulfone blood levels have been measured, following intramuscular injection of DDS suspended in oil.

"Serologic Control of Leprosy Patients Under Treatment"

Investigator: Dr. José Oliveira de Almeida, Fac. de Medicina, Univ. de São Paulo, Ribeirão Preto. This project is now receiving support from the National Institutes of Health, U.S. Public Health Service, and an application for renewal is being submitted.

Other single-country projects of current interest are those of Dr. Tomasu Imaeda of the Instituto Venezolano de Investigaciones Científicas (IVIC) in electron microscopy and of Dr. J. Convit and his colleagues, also in Venezuela, on experimental transmission of leprosy.

Proposed Multi-Country Projects

"The Pathogenesis of Indeterminate Leprosy"

Principal Investigator: to be suggested by PAHO. At the 7th International Congress of Leprology, Madrid, 1953, the present definition of "indeterminate" leprosy was adopted. There are nevertheless wide differences of opinion among leprologists in respect to indeterminate leprosy. This is reflected in the wide variations in the proportion of cases so classified.

No one knows how frequently indeterminate cases "evolve towards the lepromatous type." Patients whose disease is classified as indeterminate are regarded by some countries as potentially dangerous to the public health whereas in other countries little attention is paid to them. The object of this study is to determine the outcome of a fair sample of new cases originally classified as indeterminate - treated and untreated. A pool of cases would be established in each of several countries, e.g., Brazil, Colombia (two areas), México (two areas), and Venezuela. This project was discussed with leprologists in Rio de Janeiro and in Caracas, and was considered to be essential and entirely feasible.

"A Study of Administrative Methods of Control of Leprosy"

To be carried on by PAHO. Although the principles upon which control methods must be based are generally agreed upon, nevertheless there are wide differences between the American Republics in respect to such methods. It would be worthwhile to make a detailed study of current practice in each country with a view to obtaining greater uniformity. The trend to out-patient care is evident everywhere, but the best future use of existing leprosaria should be examined. The duration of surveillance and the frequency of examination of contacts are matters which affect the use of staff and expenditure of funds. There is no agreement on these points; even the definition of a "contact" is not uniform.

Research Training

There are no fixed lines for training in leprosy research. Leprosy problems require investigation by biologists, biochemists, biophysicists, and

other specialists. The small Leonard Wood Memorial research staff includes bacteriologists; biochemists, general and specialised in enzymology; epidemiologists, clinicians, a pharmacologist and a pathologist. There is a great scarcity of such research workers in Latin America.

The first step should be to assist certain countries in strengthening the staff of institutions in which leprosy research is now going on. In particular, a nucleus of research workers in each of these places should be supported on a full time basis.

There are also a number of institutions in Latin America where it might be possible to interest one or more staff members in certain facets of the leprosy problem. Young research workers would then be attracted to these places for training. Among the institutions are the following: Argentina - Instituto Nacional de Microbiología, Buenos Aires; Brazil - The Institute of Tropical Medicine, University of São Paulo, and the Oswaldo Cruz Institute, Rio de Janeiro; Colombia - International Center for Medical Research and Training, Universidad del Valle, Cali; Mexico - Institute of Health and Tropical Diseases of México; and Venezuela - Instituto Venezolano de Investigaciones Científicas, Caracas.

There should also be a greater interchange of graduate students than now exists among Latin American medical institutions both in research and practice. A few graduate students from other countries could be given research experience at the Institute of Leprology in Rio de Janeiro, and at the Institute for Leprosy Research in São Paulo.

There is need also for provision in the Americas for a center for teaching and research on Physical Medicine as applied to leprosy, along the lines of that at Vellore, India. A beginning is being made in Caracas by Dr. Arvelo and in São Paulo by Dr. Faggin.

PLAGUE IN THE AMERICAS*

General Background**

Plague entered Venezuela through the port of La Guaira in 1908 and soon spread to the hinterland, where rural areas first of the Miranda State and then also Aragua state became involved. To judge from the incomplete information available, it would seem that within recent years the manifestations of the disease have remained restricted mostly to the Ricaurte district of Aragua State. Undoubtedly wild rodents, two species of which have been definitely implicated, serve as the reservoir of the infection. However, the common rats and also domesticated guinea-pigs may become temporarily involved in the wild-rodent epizootics and may then be instrumental in conveying the infection to man. Since many essential details are still unknown, further studies on the ecology and epidemiology of plague in Venezuela are indicated. It would be of prime importance to establish whether really the infection is now restricted to a limited part of its original focus. For in this case a campaign against the wild rodents might be in the realm of practical politics.

The entry of plague into Guayaquil, Ecuador, in 1908 led not only to a temporary entrenchment of the infection in that seaport and its spread to many other settlements as well as to the rural areas of the coastal provinces of Ecuador, but eventually also to a penetration of the disease into the hinterland, where it still persists in the provinces of Chimborazo, Tungurahua and Cañar. The same holds true for the province of Loja, into which

*From RES 1/13 prepared by PAHO Consultants in Plague Research.
**Data on other plague-involved countries will appear in a later document.

plague infiltrated from adjacent endemic areas of Perú. In all these permanently affected provinces wild rodents form the reservoir of the infection. Several times during the recent years the disease from these sylvatic foci has led to a reappearance of plague among the rat and human populations in coastal localities. Though many studies on the plague situation in Ecuador have been made in the past, information on many essential problems is still lacking. This holds particularly true for the provinces of Chimborazo, Tungurahua and Cañar where the infection, because possibly limited to restricted areas, might prove amenable to control.

The history of plague in Perú is similar to that of Venezuela and Ecuador; the infection, entering by the maritime route, eventually became entrenched in the wild rodent populations of the interior. To evaluate the present situation in the country is most difficult because fairly up-to-date information could be obtained only for the sylvatic plague focus in the provinces of Huancabamba and Ayabaca. To what extent the infection is still active in the Lancones district adjacent to Ecuador could not be ascertained, while for the other recently affected parts of Perú really nothing is known than bare figures recording the appearance or recurrence of the disease. A country-wide appraisal of the present plague situation in Perú is therefore urgently needed. Since, however, even the scanty available information leaves no room for doubt that among the various presently plague-affected regions of Perú the Huancabamba-Ayabaca focus is by far most seriously involved, it seems legitimate, when proposing a program of plague investigations for that country, to concentrate attention upon this focus. When implementing the program, stress ought to be laid upon investigations apt to lower the deplorably high mortality in the focus.

Wild-rodent plague has become widely spread in the United States since the beginning of the present century, sylvatic plague foci having been detected successively in 15 states. However, the incidence of human plague in these regions has remained remarkably low, because as a rule man entered them but occasionally not for occupational reasons but for the purpose of camping, fishing or hunting. It has to be pointed out, however, that owing to this paucity of the attacks often the occurrence of human plague is not recognized early enough to save the patients or a diagnosis is even arrived at only after the death of the victims. It is necessary to remedy this situation by alerting the medical profession and the public.

Research Needs in Perú, Venezuela and Ecuador

Perú: Plague Ecological and Epidemiological Studies in the Huancabamba-Ayabaca Focus

1. Wild Rodents and Lagomorpha

It is planned to study the ecology of the various species of rodents and lagomorpha involved in the plague manifestations in order to delimit their habitat, establish the possible existence of strongholds of the infection, and determine the ability of the animals to approach or enter human habitations or settlements.

Systematic studies of the occurrence of natural plague in the various species of rodents and lagomorpha would be made in order to distinguish between reservoir species constantly harboring the infection and those periodically or occasionally involved. Batches of the species involved in the plague manifestations will be experimentally infected with *P. pestis* strains of standard virulence so as to determine their susceptibility or resistance to plague.

2. Fleas of the Wild Rodents and Lagomorpha

It is planned to make systematic studies to determine the occurrence and frequency of the various flea species concerned on wild rodents and lagomorpha, common rats, house-mice, and domesticated guinea-pigs, and in the various parts of the focus and at different seasons of the year. The occurence of natural plague in the various fleas would be determined with the aid of pooling tests. The vector capacity of the various flea species found naturally plague-infected would be studied, using whenever possible laboratory-bred strains.

3. Common Rats and House-mice

Systematic studies are planned to determine the prescence or absence of the two species of the common rats and of the house-mice in both the settlements and in the rural areas of the focus. It is proposed to study the occurrence of natural plague in the common rats and the house-mice by examining all animals found dead and making guinea-pig tests with the pooled organs of trapped rats. Since it has been claimed that Peruvian rats have become resistant to plague, it is planned to challenge batches of these animals, collected both in the settlements and in the rural areas of the focus, with P. Pestis strains of standard virulence.

4. Domesticated Guinea-pigs

Observations would be made on the comparative frequency with which guinea-pigs are kept in settlements and rural houses of the various parts of the focus. It is proposed to keep a watch for the occurrence of natural plague by dissecting and examining all animals found dead, and sacrificing

and examining those showing signs of illness. The blood sera of all guinea-pigs under test will be kept in a lyophilized condition so as to make them available for further exhaustive studies. It will be determined whether differences in susceptibility to experimental infection with various P. pestis strains exist between the guinea-pigs kept respectively in recently plague-affected and in plague-free localities and at different seasons of the year.

5. Intradomestic Flea Fauna

It is projected to make studies on the occurrence and frequency of the various flea species infesting common rats, house-mice, and domesticated guinea-pigs, as well as on the fleas found free-living in houses, paying special attention to the occurrence of X. cheopis, wild rodent fleas, and the various forms of P. irritans, the existence of which has recently been claimed.

Pooling tests would be made with batches of the various domestic fleas to determine the presence of plague in these parasites, particularly in localities invaded or threatened by plague, and vector efficiency studies would be made with the intradomestic flea species, particularly with the various forms of P. irritans encountered. Comparative studies are also contemplated of the action of DDT and other insecticides on the domestic flea fauna.

6. Epidemiological Observations

Systematic studies would be made on all human manifestations of plague met with by the study group. The occurrence of subclinical forms of plague would be studied with the aid of surveys in groups of the population exposed to the risk of infection. It is also planned to explore the possibility of forecasting the occurrence of human plague manifestations.

Venezuela: Ecological and Epidemiological Studies in the Plague Focus

Studies analogous to those outlined above are also contemplated for the Venezuelan plague focus. Provided that strongholds of the infection are found in the Venezuelan plague focus, a pilot study is planned to explore the possibility of sufficiently thinning out the populations of the reservoir species in these localities as to cut short the spread of plague. Consultation with wild-life experts would be indispensable to devise methods suitable for such a temporary reduction of the populations; a method which, as proven by experiences in the Soviet Union, is effective in plague control.

Ecuador: Ecological and Epidemiological Studies in the Plague Foci

In view of the involved plague situation in Ecuador it is proposed to postpone the framing of a program for studies in that country until experience on the suitability of the plans contemplated for Perú and Venezuela has been obtained.

Since the proposed investigations are not merely of academic interest but serve practical ends, research would always be directed towards the ultimate goal of providing the knowledge and tools to permit the national plague prevention services to deal with imminent or actual manifestations of the disease in man. Attention would be paid in particular to studies on the possibilities of preventing human plague not only by the use of insecticides (see above under "Perú") but also with the aid of potent synergist vaccines in basic and booster doses and, whenever indicated by local emergencies, through administration of antibiotics or sulfonamides. The therapeutic use of

these substances would likewise be studied as much as possible so as to arrive at a fully effective yet simple and economical scheme of treatment.

RESEARCH AND RESEARCH NEEDS IN THE ARTHROPOD-BORNE VIRUS DISEASES IN LATIN AMERICA*

Two classical epidemic arthropod-borne virus diseases, urban yellow fever and dengue fever, have been conquered in the Americas. These advances were made largely through intensive control programs designed to eradicate urban vectors or to immunize exposed human populations. It must now be recognized, however, that these two diseases and the programs for their study and control are only initial aspects of a much larger problem in this field.

Current Status of Knowledge and Unsolved Problems

Sixty-eight arthropod-borne viruses are currently known to exist in the Western Hemisphere. Ten viruses have caused human epidemics and five have produced epizootics in domestic animals. Human encephalitis caused by up to six different arthropod-borne viruses occurs in 13 of 24 countries in the Western Hemisphere and the failure to recognize this disease syndrome in certain other countries is undoubtedly related to the absence of viral investigations. Yellow fever continues to occur in an enzootic jungle cycle in tropical countries and its geographic extension remains a threat to adjacent regions. In 1958, hemorrhagic fever, apparently mite-borne, rose to epidemic proportions in rural Argentina near Buenos Aires. An antigenically related virus exists in Trinidad and the possibility of a more northern distribution of this disease must be considered. At least 15 arthropod-borne viruses pro-

*From document RES 1/9 prepared by Consultants from the staff of the School of Public Health, University of California, and the School of Medicine, University of Minnesota following their field trip, April-May 1962, to México, Panamá, Colombia, Perú, Chile, Argentina, Brazil and Trinidad.

duce mild to moderately severe febrile illnesses in man and one of these viruses is related antigenically to Naples sandfly fever virus. Animal diseases also result from infection by arthropod-borne viruses. Epizootic equine encephalitis caused by three different arthropod-borne viruses exists throughout the entire Western Hemisphere, and recent isolations of vesicular stomatitis viruses from arthropods suggest that this economically important disease may involve arthropod transmission. Also blue-tongue virus, transmitted by Culicoides, exists in the U.S.A.

In addition, it is probably that:

1. Considerable number of human cases of febrile disease in the tropics, currently of unknown etiology, are caused by arthropod-borne viruses;
2. There are arthropod-borne viruses as yet undiscovered in the Americas;
3. The geographic distribution of many viruses is much wider than presently recognized.

Thus, the importance of these viruses in human and animal health has yet to be fully evaluated. The occurence of epidemics caused by newly discovered arthropod-borne viruses (e.g., hemorrhagic fever in Argentina, Oropuche fever in Belém, and Mayaro fever in Bolivia and Brazil) indicates that the diseases the ARBO viruses cause are not limited to the well-known arthropod-borne viral encephalitides, yellow fever and dengue. Moreover, the continued occurrence of encephalitis epidemics and equine epizootics indicates that much still remains to be learned about these viruses.

Major unsolved research problems related to arthropod-borne viruses in the Western Hemisphere include:

1. Full evaluation of their importance in human and animal health;
2. Knowledge of their geographic distribution and thus their danger to humans and domestic animals moving into unsettled areas;
3. Recognition of virus types (new representative viruses are still being discovered throughout the Americas);
4. Understanding of the natural cycles for each virus;
5. Evaluation of the possibility of geographic movement of viruses by migratory birds, humans, domestic animals, vectors, airplanes, etc;
6. Development of effective control and therapeutic measures.

Current Research Activities

Although more arthropod-borne viruses and their related diseases exist in Middle and South America than in North America, the majority of research laboratories in this field are currently located in the Northern part of the Hemisphere. Over 50 virologists, 30 entomologists and 15 zoologists are now involved in arthropod-borne virus research in Canada and the United States whereas throughout Latin America there are only approximately 38 virologists, 18 entomologists and 6 zoologists working in this field of research. In Canada and the United States, most provincial or state laboratories offer routine diagnostic services for these diseases whereas similar services are almost non-existent in Middle and South America, except in scattered research laboratories. In addition, space, equipment and experimental animals are often inadequate in quantity and quality to meet research needs.

Despite the scarcity of trained personnel interested not only in virology but especially in entomology and zoology, and limitations in facilities, considerable research is underway or being initiated throughout Latin America. Studies are chiefly oriented toward discovering which arthropod-borne viruses exist in different countries, and relating them to human disease. In Panamá, Belém, São Paulo and Trinidad, staff and facilities allow considerable additional attention to be given to ecologic studies.

Recommended PAHO Activities in Research

During this survey suggestions were expressed by research workers and and administrators concerning appropriate areas of PAHO activity, essential to further development and improvement of arthropod-borne virus research.

From these suggestions the consultants recommended that the following activities receive priority consideration:

Exchange of Information Among Research Workers

1. Development of a continuing system of annual or biannual informal meetings of active workers in the Americas should be considered a vital PAHO activity. As a beginning, PAHO should consider the organization of an informal meeting for exchange of information among active workers in arthropod-borne virus research in Latin America at the time of the seventh International Congress on Tropical Medicine and Malaria, to be held in Rio de Janeiro on 1 - 11 September 1963. A similar meeting at the last Congress in Lisbon in 1958 was highly successful and of great assistance in formulating the current WHO program.

2. PAHO should assume responsibility for bringing new research

groups into association with the current world-wide Information Exchange and Arthropod-borne Virus Catalogue activities and should offer whatever support is required to assure effectiveness of these forms of information exchange. The current Information Exchange activities should be continued in their present informal and unpublished format.

3. PAHO should make regular contributions to the Information Exchange by providing current information regarding arthropod-borne virus epidemics and epizootics, development of new laboratories, availability of Reference Centers, etc., in the Western Hemisphere.

Training of Research Personnel

1. Development of short term intensive courses in basic laboratory and/or field techniques, particularly at regional centers (see Recommendation 3 below). These could be patterned after the present PAHO training activities of the Aftosa and Zoonoses Centers and should be based on students performing procedures rather than merely viewing demonstrations.

2. Placement of research workers and educators in Middle and South American laboratories to train local personnel. An example is the current PAHO enterovirus training program at the Oswaldo Cruz Institute in Brazil. University faculty on sabbatical leave might also be interested in this activity.

3. Development of agreements with institutions carrying out active research programs in Latin America for acceptance of well-prepared trainees for periods of at least 6 months to 1 year to obtain further laboratory and field training by active participation in field and laboratory research programs.

4. Similar agreements for shorter training periods are also needed, but they should be limited to learning specific techniques essential for immediate incorporation in a current research project.

5. For people who are to be or are already responsible for research programs, one or more years of advanced study in an educational institution obtaining advanced training in a special field. Training outside of Latin America will be required for many of these persons, but only experienced, highly capable and mature individuals should be selected.

6. Research workers, instructors or technical personnel of PAHO should participate in an intensified follow-up system, to visit the trainees in their laboratory or field program area, to review their success in utilizing the training provided, and to assist them in solving problems which may develop.

Development of Regional Reference and Training Center or Centers for South and Middle America

It is recommended that early consideration be given to the establighment of a Center in São Paulo, Brazil, in collaboration with the Institute Adolfo Lutz and the School of Hygiene and Public Health. This location has the following advantages:

1. Geographically, it is centrally located to serve Argentina, Chile, Brazil, Uruguay, Paraguay and Bolivia and it has excellent air transportation connections to these areas and to most northern areas. This region is the most isolated with respect to existing reference centers.

2. The Instituto Adolfo Lutz has an excellently equipped and housed virologic research unit, which is active in arthropod-borne virus research. The administration of the Institute is sympathetic to increased

research and service functions, and there is adequate financing of the local activities on a current basis.

3. There is reason to believe the Director of the Institute would effectively support the establishment of a reference center.

4. There is an active program of medical entomologic research and teaching in the School of Hygiene and Public Health, which offers a service and training facility essential to a reference center.

5. There are facilities for microbiology teaching in both the School of Hygiene and Public Health and the Medical School, which could be used for short-term courses in virus laboratory procedures.

6. There are good library facilities covering literature in virology and medical entomology.

7. There is a combined atmosphere of active research and academic programs in virology, entomology and vertebrate zoology which are essential to a reference center type of activity.

8. Almost all of the arthropod-borne viruses that are currently known in South and Middle America have been recovered in Brazil, and thus can be worked with in this country with a minimum of restrictions on importations.

9. Field areas, where arthropod-borne viruses are active, are readily available within short distances of the city. This offers opportunities for field training, demonstrations of investigative procedures, and the development of short or long term participation of trainees and fellows in active research projects on virologic, entomologic or vertebrate aspects of investigations.

The proposed center would require the obtaining of adequate labora-

tory space to house the virologic aspects of the reference center. As in the beginning this activity will be concerned primarily with the identification and characterization of a wide range of viruses and preparation of antisera, it should be separated physically from the existing field investigative unit of the Institute, which is currently isolating new strains of virus from the field.

At the onset, personnel should include one or two competent virologists interested in the identification and characterization of arthropod-borne viruses and two to four competent technicians and three to five supporting personnel for animal care and other auxiliary services. Later staff needs may include an entomologist, a vertebrate zoologist and an epidemiologist, and will be dependent on the demonstrated needs for such staff to carry out service or investigational activities in the region. Equipment needs are those standard for a virologic laboratory and do not include numerous expensive or specialized items. Training courses would, of necessity, require supplementary personnel for the time they were in session. It would be anticipated that staff could be available as consultants from the several active research centers in the region.

While interest and needs were expressed for a regional reference laboratory in Northern South America or Middle America, the majority of the present laboratories in these regions are self-sufficient at this time, are closely allied with parent laboratories in North America, or are effectively exchanging reference material on a current basis. The Middle America Research Unit (MARU) of the USPHS may serve in part as a sub-regional laboratory for the surrounding area if sufficient staff is assigned that are competent in virology and the necessary biologic fields. It is not prepared to do so

currently. None of the other laboratories that were visited offered sufficient space, interests in this type of activity, coverage of the necessary fields for services and training, stability of personnel, or other potentials to be given serious consideration as a regional center at this time.

Provision of an Intermediary Information Service Between Investigators in Latin America and Granting Agencies in the United States or Other Countries

1. PAHO might offer services for translation of grant application from Spanish or Portuguese into English;

2. Properly oriented PAHO staff might offer guidance and assistance to Latin American research workers to assure proper and complete understanding of the material expected in specific sections of research grant applications;

3. PAHO staff could assure understanding of the specific types of research which are acceptable for support by granting agencies.

Facilitation of Investigations of Epidemics

PAHO can assist by:

1. Stimulating Ministries of Health and Agriculture to welcome and support, such investigations;

2. Organizing international and national rosters of individuals and agencies capable of and interested in making such investigations, and inviting them to do so;

3. Obtaining and maintaining a small reserve fund to finance transportation and field subsistence of investigators sent on such research missions;

4. Facilitating movement of investigators across international boundaries.

Assistance in Rapid and Uninterrupted Movements of Scientific Specimens Between Countries and to Reference Centers

PAHO should develop a scheme to accomplish this objective.

Development of Improved Diagnostic and Reporting Systems

1. A joint endeavor by PAHO and FAO to assure that public health and veterinary health agencies promptly report and support investigations of outbreaks by research groups is badly needed.

At the present time, the only data which is published is that reporting large outbreaks or sporadic cases from which a virus is isolated that is new for a geographical area. All other records are lost or buried in laboratory files. Full recognition or evaluation of the public health or veterinary importance of this group of agents will be dependent on a constantly increasing level of awareness of their potential importance and increased application of diagnostic measures to suspected cases.

2. It is suggested that some mechanism should be developed for an annual computation of the confirmed human and animal cases that are diagnosed by the research and diagnostic laboratories. These data are lost or become diluted in official morbidity and mortality statistics (except for yellow fever). An expression of interest in such computations would be concrete evidence of support of the laboratory programs and would stimulate increased activity and utilization of such facilities.

The above suggestions are compatible with prior suggestions in Tech. Report No. 219 of WHO and Scientific Publication No. 53 of PAHO in considerations of the same problem.

Utilization of the Foot-and-Mouth Disease Center

Arthropod-borne virus research units in Middle and South America should be notified of the availability of virus identification services for the vesicular stomatitis viruses at the Foot-and-Mouth Disease Center in Rio de Janeiro. Field laboratories have been making increased numbers of isolations of viruses in this group and have had difficulty in their identification and characterization, but they have not effectively utilized the services of this regional center, which are excellent.

Support of Present Research Units

While the number of research groups concerned with arthropod-borne viruses in South America is limited, these consultants did not feel there is an urgent need for a program to accelerate development of additional new research groups or organizations. It is undoubtedly of more importance to encourage the continuation of interests of the present groups, to assist them in obtaining adequate financial and administrative support and stability from their parent organizations, and to assure adequate training and reference center support for the present and future personnel of these units.

Perú is the only country which may be an exception to the above, and a new research group is presently being trained and organized to fill the need for this area. Those countries that have no active research programs have been receiving attention from established research groups. Studies in Ecuador have been supplemented by Colombian research units. The Middle America Research Unit is making exploratory surveys in Bolivia and this group is willing to perform studies throughout Middle America. Paraguay and Uruguay could be and have been assisted by laboratories in Argentina. The Guianas are covered by the Trinidad Regional Virus Laboratory.

Inevitably, additional universities and research institutions will become interested in arthropod-borne viruses and should not be discouraged. Support of such new groups by PAHO should be concerned primarily with training, consultation and advice and assistance in recruitment of personnel. Such new research units may wish, initially, to orient their activities toward serologic surveys. PAHO should encourage this attitude, but should emphasize, that, to be meaningful, arthropod-borne viruses serologic surveys must be followed by isolation of viruses and by ecologic studies.

Collaborative Studies in the Amazon Basin

PAHO should encourage collaborative studies by groups interested in the Amazon Basin in an effort to consolidate knowledge of the distribution of viruses in this area and the similarities or differences to be found in arthropod vectors and vertebrate hosts in the areas that have been studied.

The Amazon Basin comprises one of the largest underdeveloped land masses in the world. Studies of the arthropod-borne viruses along the periphery of this area clearly indicate that this Basin, with its particular ecologic characteristics, is unusually suited for the enzootic maintenance of a large number of arthropod-borne viruses. Existing research units in Bogotá and Cali, Colombia, the proposed unit in Lima, Perú, the University of Cordoba in Argentina, the Institute Adolfo Lutz and Belém Virus Laboratory in Brazil provide a circle of active research groups all with an interest in future research work in various portions of this Basin and its adjacent regions.

In addition, human population groups are being moved into this Basin in increasing numbers by the Brazilian and Peruvian Governments. These largely susceptible populations offer unique opportunities for epidemiologic studies of a wide variety of infectious and non-infectious diseases. PAHO, by

arrangements with the various governmental agencies, should make every effort to assure that competent and interested research groups have an adequate opportunity to make such studies of these pioneering groups.

Extensive ecologic studies are indicated to consolidate the knowledge of arthropod-borne virus distribution and movements in the Amazon Basin. These studies will have to include professional workers from the fields of entomology, vertebrate zoology, botany, climatology and geography as well as virology. Establishment of such studies cannot be planned at the present time; however, they should be anticipated. A vast array of altitudinal, climatic and floral habitats are encompassed in this area. Final understanding of the natural cycles of arthropod-borne viruses, limits on their distribution and dissemination, and the utilization of this land mass for human habitation and development without undue risk of disease, will be dependent on such ecologic studies. Similar studies in other basins, such as those of the Orinoco and Paraná rivers could be considered when conditions for such investigative efforts appear promising.

A specific example of a study requiring international research coordination and cooperation is that of the movements of birds along the eastern slopes of the Andes, and along the Atlantic Sea Coast and the degree to which interchange occurs across the vast expanses of the Amazon Basin. It has long been suspected that bird movements might be effective in the dissemination of these viruses, but indisputable evidence awaits further collaborative investigations.

RESEARCH NEEDS IN THE ZOONOSES IN THE AMERICAS*

Rabies

Rabies continues to be a public health problem in North, Central and South America, as well as in other areas of the world. Some significant advances have been made in rabies investigation and control during the past 10 - 15 years, and yet there are still many problems which must be solved before rabies can be conquered. Investigations can best be outlined when placed in the proper public health perspective; first, human rabies control, second, domestic animal rabies control, and third, wildlife rabies control.

Human Rabies Control

The decrease of human rabies cases in North America and some of the Latin American countries is encouraging. This is due to the development and use of good animal vaccines combined with stray dog control, quarantine of suspected and biting animals, and public education concerning care and handling of animals. Still, there are thousands of individuals who each year receive post-exposure rabies treatment due to the continued existence of large numbers of rabid animals, and other thousands who needlessly take the treatment because methods of handling and diagnosing rabies are inadequate.

Several important questions regarding pre-exposure immunizations indicate the need for more work:

1. What is the relationship of serum neutralizing (SN) antibody following duck embryo vaccine (DEV) to protection against rabies virus? In

*From document RES 1/16 compiled from the literature and other sources by a group of PAHO consultants.

animals it is possible to assess this with known doses of challenge virus.

2. How often should boosters be given to insure continued protection against rabies?

3. When a person who is known to have had a titer is bitten by a rabid animal several months later, how many doses of vaccine are then required?

4. A laboratory problem closely associated with the one of pre-exposure is development and evaluation of a faster test for determining the presence of protective antibody. The indirect fluorescent antibody procedure, tissue culture, gel diffusion, hemagglutination and complement fixation (CF) tests might well be adapted for this need.

Rabies Control in Domestic Animals

Dogs continue to be the most commonly rabies-infected domestic animal in spite of proven methods to control rabies in this species. The low egg passage (LEP) chick-embryo Flury strain of rabies vaccine was developed in 1951 and duration of immunity was shown to last at least three years. It has been estimated that if 70 per cent of the total dog population of an area is immunized against rabies, dog rabies can be easily controlled. Stray dog control and, in some instances a quarantine of dogs, are further necessary control measures which must be practiced.

The safest vaccine for use in cats is the nervous tissue vaccine (3 ml of a 20 per cent suspension) although high egg passage (HEP) can also be used (1.5 ml of 33 per cent suspension). HEP is also used for puppies, pet skunks, and such farm animals as cattle and horses. The animal vaccination problem would be simplified, and the cost reduced, if one vaccine, effective in all animals, could be developed.

Wildlife Rabies Control

At present, the only practical method of control of wildlife rabies is to initiate a reduction program of the species of wildlife involved within a given area. The aim of this program is to thin out the wildlife population so severely that a rabid animal does not contact another before dying and thus the rabies virus dies out. In parts of northern Mexico effective programs have been conducted, with the assistance of the Pan American Sanitary Bureau and the U.S. Fish and Wildlife Service, wherein the wolf and coyote populations have been so reduced that rabies disappeared.

Research is needed in an effort to understand the natural history of the disease before more scientific control of wildlife rabies can be practiced. Considerable work has been done in the past four years in the U.S. in foxes, skunks, raccoons, opossums and bats. The fox has been found to be the most susceptible species. In three separate studies, less than 10 mouse LD_{50} were required to kill 50 per cent of the foxes inoculated intramuscularly. The skunk and raccoon required 500 - 1,000 mouse LD_{50} of the same fox salivary gland virus to become infected and opossums have been the most resistant species of terrestrial mammals when inoculated intramuscularly. Skunks, regardless of size of inoculum, generally emitted more virus in their saliva than any of the species checked. Foxes given larger doses of virus (greater than 1,000 mouse LD_{50}) generally did not emit rabies virus in their saliva and they had a shorter incubation period than those given lower doses (less than 1,000 MLD_{50}). Thus there are species differences among the animals regarding susceptibility and emission of virus which are undoubtedly partly the reason for the various epizootiological conditions which exist in various areas.

Within an area where rabies exists in wildlife, more detailed, controlled experimental work should be done using indigenous species and native virus to inoculate the normal animals for an understanding of the rabies pathogenesis in such host animals.

It is felt by some investigators that the Viverridae and Mustelidae are the important reservoirs of rabies virus in nature. Whether the virus has become adapted to animals such as the spotted skunk and weasel and is altered to the extent that it is not pathogenic except under stress conditions is not known. Thus, complete studies in these animals to incriminate them as "silent" carriers of rabies virus should be undertaken.

Bats undoubtedly play an important role in the dissemination of rabies virus. In many countries in the Americas bat rabies is a serious economic or health problem. Recently, it was shown that bat rabies virus can be transmitted in an aerosol to normal foxes and coyotes. By cage design, these animals were exposed only to the air in caves where hundreds of thousands of insectivorous bats were housed. Of considerable interest was the fact that none of the skunks, raccoons, cats, dogs, ringtail cats or opossums developed rabies; only the foxes and coyotes.

It is important at this point to explore further:

1. Differences in susceptibility of species with homologous and heterologous virus by various routes of inoculation;
2. Methods of virus dissemination from bats to other animals, and among bats;
3. Infection and immune rates of bats before they migrate;
4. Relationships between insectivorous and vampire bats, as well as between each of these and terrestrial mammals.

Ultimately, we need to know whether the rabies virus in these species is being altered within a species to make the public health problem worse. Until the wildlife rabies problem is studied more from both field and laboratory, it will be impossible to think of continued control or eradication of this disease.

Leptospirosis

During the past decade, much knowledge has been gained regarding the prevalence and distribution of leptospiral infections in man and in domestic and wild animals, as well as the epidemiology of these infections in many different areas of the world. This progress can be accounted for, in part by basic research studies of many workers which have contributed to the development of simpler and more reliable diagnostic methods, the availability of these procedures in more diagnostic laboratories, and to their broad application in epidemiological investigations.

Due to our knowledge of the epidemiology, the practical methods now available, and to the technical resources in most Latin American countries, efforts could best be directed towards research problems of an applied nature: 1) to obtain more secure information as to the true prevalence of infection, the infecting serotypes present, and the distribution of these types; 2) to collect data regarding factors that influence the spread and distribution of the disease and to correlate these with similar information from other geographic areas; and 3) to apply the acquired knowledge in the development and evaluation of preventive and control measures. Information obtained by such studies could be used, also, in the development and evaluation of a suitable vaccine or vaccines.

Interest in this problem exists in most Latin American countries; some have established programs. The Pan American Zoonoses Center could provide assistance through training of personnel where needed, consultations, and as a reference laboratory.

Brucellosis

Several thousand human brucellosis infections occur annually in South America. In many areas infection is primarily following occupational exposure to infected cattle, particularly in abattoirs. Infected swine play a significant role in Argentina and Brazil. Goats provide a most important reservoir of human infection, primarily by means of the consumption of contaminated fresh goat cheese.

Limited use of strain 19 in cattle in three countries, and the successful demonstration of the value of the elimination of reactor goats in another, were the only active animal brucellosis control measures noted.

It is recommended that the use of strain 19 vaccine in cattle be expanded, efforts to eliminate reactor goats be made where possible, and pasteurization of goat milk to be used in cheese manufacture be instituted.

Parasitologic Zoonoses

Trichinosis

The epidemiology of trichinosis in Central and South America is not well understood and should be investigated by modern immunodiagnostic techniques (serologic and skin tests). Incidental trichinosis in Mexico and Honduras, and endemic trichinosis in Argentina, Chile and Uruguay have been

reported in the literature. However, the prevalence of this parasitic infection in Central and South America is not known and should be investigated. We do know that in South America, trichinosis is not indigenous in Venezuela and Brazil.

Hydatidosis

The incidence of hydatid disease due to E. granulosus has been well documented in Rio Grande do Sul, Brazil, and in Argentina, Uruguay, Venezuela, Chile and Peru. In the northwestern part of North America hydatidosis is known to exist but this is thought not to be due to E. granulosus. In the southern part of North America the cyst has been reported in swine but only rarely in man.

Frequently the disease is not diagnosed. Better diagnostic techniques need to be developed and the medical professions acquainted with their use. Serologic methods for the diagnosis of hydatid disease by hemagglutination and complement fixation reactions have been evaluated and are available. Standardized antigen and control serum should be prepared by a central laboratory and distributed widely in the Americas. This program would enable hospitals and clinical laboratories to perform diagnostic tests for hydatid disease in endemic areas. Research on the development of a standardized skin test antigen (evaluation of specificity and sensitivity) and the distribution of such an antigen would be very helpful in the diagnosis of hydatid disease. With a standardized skin test antigen, studies on the prevalence of infection could be carried out.

Research on the development of serological techniques to detect infection in dogs is necessary. Large-scale screening programs should be carried out to determine an effective taeniacide for mass treatment of dogs.

Cysticercosis

The prevalence of cysticercosis is practically unknown in the Americas. Deaths due to this parasitic infection in Mexico are said to equal those due to amebiasis. A program for the evaluation of serologic techniques for the diagnosis of this disease should be initiated. Antigens must be prepared and evaluated. A skin test should be developed for the diagnosis of cysticercosis in swine. Epidemiologic studies should be made to ascertain the prevalence of T. solium in man and a mass campaign initiated to effect treatment of infected individuals.

Filariasis

The prevalence of filariasis due to Wuchereria bancrofti, Mansonella ozzardi, Onchocercus volvulus and Acanthocheilonema perstans in the Americas is high. The problem of control is serious and provided sufficient funds are available control of this disease should be undertaken. A great deal of experience and knowledge on the epidemiology of bancroftian filariasis, on control of vectors and on treatment has been accumulated in the Pacific and in Africa. Pilot projects in British Guiana, North Brazil and other areas endemic for Wuchereria bancrofti should be initiated. Studies on ecology and epidemiology of Mansonella ozzardi and Acanthocheilonema perstans should be initiated. These parasites infect millions of people in the Americas and for a small percentage of individuals, clinical disease results. Studies on the ecology of the simulium vector of O. volvulus should be encouraged in the endemic areas in Venezuela, Guatemala and Mexico. The possible distribution of simulium vectors into Colombia, Peru and the Amazon basin indicates the need for additional epidemiologic work.

Visceral Larva Migrans

The epidemiology of visceral larva migrans is not completely documented. Since the prevalence of Toxocara canis is very high in all countries of the Americas, the prevalence of disease caused by this parasitic infestation may also be high. For epidemiologic studies, evaluation of the clinical syndrome should be made.

Serologic studies for the evaluation of visceral larva migrans should be supported. Specific and sensitive tests for the diagnosis of visceral larva migrans are needed.

The problem of cutaneous larva migrans caused by hookworm larvae of animal and human origin should be investigated. Specific therapy for killing larvae in the skin should be developed.

Leishmaniasis

The problem of leishmaniasis in the Americas has not received the attention that this important parasitic disease warrants. An institute devoted solely to the study of this disease on a continental basis is required. In this institute studies on the epidemiology of visceral as well as cutaneous leishmaniasis should be carried out for the Americas. Entomological studies on vectors of leishmaniasis, studies on the diagnosis of leishmaniasis, characterization of strains and clinical manifestations, modes of transmissions, vaccination and immunization and animal reservoirs should be made.

RADIATION AS APPLIED TO MEDICAL AND PUBLIC HEALTH RESEARCH*

In order to consider the areas of research related to radiation a Scientific Group on Research in Radiation was convened in Washington in May 1962. Its report is summarized in part I, below. To further examine the areas delineated by the Scientific Group and possibly uncover other useful avenues of research one of the members of the Group, acting as a consultant, traveled to Venezuela, Brazil, Chile and Peru immediately after the Group's meeting to visit various research laboratories and hold conferences with researchers in different fields where radiation might be employed. His report appears in part II.

I. Summary of Report of the Scientific Group on Research in Radiation

In approaching its task the Group examined five areas of activity as possible broad topics which might be worthy of consideration: —

1. The Application of Radioisotope Tracer Techniques in the Study of Nutrition and of the Mechanism for Production of the Anemias Observed in Latin America

Absorption of iron and its loss through excretion

The employment of double-labelling techniques utilizing iron-55 and iron-59 developed by Finch and others could be very effectively employed in studying the absorption of iron in diets peculiar to various countries within the Hemisphere. The elucidation of this information is important for an under-

*From document RES 1/14 comprising the report of the Scientific Group on Research in Radiation and the report of the PAHO Consultant on Radiation Research.

standing of the possible reasons for anemias observed in various Latin American countries - as proper utilization of iron may be interfered with for reasons not adequately understood at present. It is also important to determine the amount of iron loss through bleeding into the gastrointestinal tract because of parasitism as well as to determine how much iron is lost in the sweat in hot and humid enviornments. Radioisotope techniques are almost ideal to assess such losses.

Relationship between calcium content of the diet and osteoporosis

By using calcium-45 as an isotopic tracer it may be possible to elicit information which might help to explain why osteoporosis apparently does not occur under certain conditions of low calcium intake.

2. The Application of Radioisotope Tracer Techniques in the Study of the Nutritional Requirements of Tropical Disease Agents and in Studies of the Effects of Tropical Diseases on the Biochemical and Physiological Functions of the Host

Metabolism of the parasite

The use of radiocarbon and tritium-labelled compounds offer possible avenues of approach in elucidating the metabolism of these agents - as it is possible that some peculiarity in the metabolism might be used in providing an approach to the therapy of the disease which they cause.

Metabolic activities of the host

Radioisotope techniques already applied to the study of kidney function, hemopoiesis, electrolyte metabolism and balance, hemoglobin synthesis and destruction, etc., might be important in understanding the mech-

anisms responsible for the manifestations of the tropical diseases and in devising better techniques for therapy.

3. The Application of Radioisotope Tracer Techniques for Studying the Biology and Ecology of the Vectors of Parasitic Diseases; and the Application of Ionizing Radiation for Sterilization of Vectors or Intermediate Hosts with the Purpose of Reducing Their Population

Biology and ecology of vectors

Radioisotope techniques furnish a powerful tool for such investigations by labelling the vector and studying its distribution, motility range, its habits and many reproductive characteristics.

Sterilization of the male vector by irradiation

The successful application of this technique to the elimination of the screw-worm fly (Callitroga hominivorax) provides an opportunity for testing the same method in a selected number of disease vectors. Preliminary information already indicates the possibility of species elimination by mating irradiated sterile males with the wild fertile females for some of the Chagas' disease vectors.

With the cooperation of two members of the Group (Drs. Roche and Baldwin) a project was drafted for later submission to the NIH to study in detail the reproductive behavior and the ecology of the Rhodnius prolixus, the vector of Chagas' disease in Venezuela. The research project envisages a cooperative arrangement wherein the Instituto Venezolano de Investigaciones Científicas (IVIC) will carry out all the ecological studies and the laboratory of Dr. Baldwin at the Atomic Energy of Canada Limited will carry out all the histological studies. Both laboratories will conduct observations on

reproductive behavior of the vector as well as determine the effects of sterilizing doses of irradiation on the male and its subsequent action on species reduction or elimination in laboratory controlled studies. Assuming the latter are successful it is contemplated moving the study to a semi-natural environment and finally conducting a field pilot program on a presently uninfested island at Lake Valencia in Venezuela.

Attenuation of parasites by irradiation to produce an immunizing agent

The aim here is to reduce the pathogenicity of the parasite but retain its antigenicity for evoking the immune response. Work is already proceeding along these lines with Schistosoma mansoni.

Irradiation to sterilize an intermediate host

Work now being carried out at the NIH on the snail gives some promise that such an approach would be fruitful in breaking the cycle for Schistosoma mansoni transmission.

4. Study of Possible Biological Effects on Human Population of Increased Background Radiation Due to Increased Cosmic Radiation at High Altitudes or to Abnormally High Levels of Radioactive Elements in the Ground (e.g. monazite sand areas of Brazil which contain comparatively high levels of thorium)

The group felt that inadequate population samples and poor vital statistics precluded satisfactory research in this area at present.

5. Studies on the Leukemogenic or Carcinogenic Effects of Radiation Used in the Therapy of Various Diseases

The Group, while mindful of the potential value of this research,

thought an improvement in vital statistics and more information as to the incidence of radiation-induced disease following treatment with ionizing radiation of various conditions was needed in Latin America before such research could be considered profitable.

II. Summary of Consultant's Report

The consultant's Latin American visits indicated much interest on the part of different research workers and the possibility of conducting studies in the following areas:

1. Projects Utilizing Radiation as a Tool in Studying Pathophysiology of Disease

Manganese poisoning

Certain Chilean researchers indicated interest in this serious clinical and public health problem present in the Chilean manganese mines. A cooperative effort with a researcher at the Brookhaven National Laboratory in Long Island, New York, using neutron activation analysis for measuring manganese concentrations was proposed.

Lead poisoning

This being a serious problem in both Peru and Chile much interest was shown in both countries in the possibility of establishing a research project in this area. The proposed project would aim at studying the kinetics of erythropoiesis in lead poisoning and the effects of altitude thereon (the latter in view of the location of some of the lead mines in Peru). In addition to routine hematologic studies, isotope studies using iron-59 to deter-

mine radioiron turnover, chromium-51 for studying red cell survival and tritiated thymidine for determining uptake by bone marrow. As electron microscopy would also become a necessary part of such a project it is contemplated collecting the bone marrow speciments in the participating countries in Latin America and forwarding them to the cooperating laboratory in the United States for study.

Localization of hydatid cysts of the liver

A simple technique for early recognition and localization of the cysts would be of obvious clinical importance as it would permit earlier and more effective surgical intervention. The possibility exists for developing such a method using isotopic concentration techniques followed by scintillation scanning procedures. Much interest was shown in this problem at both Porto Alegre, Brazil, and Santiago, Chile. Preliminary discussions have already been entered into between a researcher in Chile (who has access to clinical cases) and another at the University of California. Both are conversant with the techniques required for such study.

Iron absorption and excretion

Anemia as produced by hookworm and other diseases constitutes a significant problem in many areas of Latin America. Detailed studies of the kinetics of erythropoiesis in the anemia stage as well as after response to therapy is fundamental. Iron metabolism must also be studied. These studies should include measurement of red cell production and loss with radioiron and radiochromium, in vitro tritiated thymidine studies, cell sizing, etc. Intestinal iron absorption and iron loss should also be studied using radioiron. In connection with iron loss the importance of the sweat as a channel

of such loss in iron deficiency in high and low humidity areas could readily be determined by means of radioiron and whole body counting.

Study of the ecology and biology of the vectors of Chagas' disease using radioisotopes and possible control of the disease by irradiation sterilization of the vector

Much interest was expressed in this project and in Peru a willingness to cooperate in such a program was indicated.

Endemic goiter

This is a problem throughout Latin America but even though the study of it utilizes isotopic techniques it was considered to be primarily a subject for investigation by the endocrinologist rather than the radiation group.

2. Research on Radiation Effects

A study of aplastic anemia in burros

Evidence appears to suggest that a lowering of the body's oxygen tension may provide a degree of protection from ionizing radiations. Therefore, it would be valuable to study the effect of altitude on bone marrow function as well as studies of the occurrence of late aplasia in the irradiated burro. These projects, coupled with a study of the radiosensitivity and effect of altitude thereon in animals indigenous to higher altitudes, would constitute a most important research endeavor in order to determine some of these relationships in man. The veterinary and medical schools in Lima are most interested in such a project which would involve studies with iron-59 turnover and chromium-51 survival techniques.

3. Epidemiologic Studies

The relationship of genetic and somatic effects to high natural background radiation has been the subject of wide interest for many years. However, the obvious difficulties, e.g. suitable control populations of similar ethnic origin in low background areas, accuracy of diagnosis, size of population sample, case follow-up, etc., make such epidemiologic studies difficult. Initially, it was recommended that the present physical measurement work being carried on in Rio de Janeiro be extended and that this be followed by detailed studies of radionuclide contamination of food, milk and water supplies. There is also need to evaluate the body burden of isotopes in the high background radiation areas, such as among the workers in the monazite sand separation plants of Brazil where thorium contamination is present. This might eventually open a way for evaluation of somatic effects.

RESEARCH NEEDS ON THE ECONOMICS OF HEALTH AND MEDICAL CARE IN LATIN AMERICA*

Introduction

The economic aspects of health services and medical care have received increasing attention in recent years in the American countries. A variety of analyses of health and medical services have been made in an attempt to formulate optimum conditions of hospital organization, private and social insurance, and medical practice. Other studies have been concerned with costs, prices, the financing of health care, and comparisons of systems.

The situation in Latin America can be characterized as one of scarce resources. In many areas there are shortages of personnel and problems of unequal distribution of facilities. With low real income per capita, countries are short of funds for health. Basic statistics are often inadequate, and the health economist must undertake direct investigation of problem areas to supplement official data.

Economic theorists have demonstrated that there is a close relationship between health and economic progress - one potentiating the other - but precise quantitative measurements have not been possible for lack of information. Information is also lacking to direct health efforts to those areas of activity which can make the greatest contribution to economic development, and to show health officials which economic development programs are likely to make the greatest demands on health services.

At the Conference on the Economics of Health and Medical Care spon-

*From document RES 1/3 prepared by the economic advisor of the PASB.

sored by the United States Public Health Service and the University of Michigan in May 1962, it was recognized that health economics fell naturally into two main areas of study - the internal organization of health care, and the relationship between health and the general economic context. In the developing countries, the latter was of greater interest. Health economists, in the words of the Michigan Conference, "are attempting to apply economic concepts and methods of analysis to problems of health - such problems include the economic dimensions of decisions as to the allocation of resources to health improvement and maintenance - methods of financing access to medical care - forms through which medical care is supplied."

The subjects on which research by health economists in the Americas promises to be most fruitful are the provision of basic information on costs and benefits which will enable cost-benefit analysis to be undertaken, the economic dimensions of different systems of health care, such as integrated health services, and the allocation of resources to health in the context of general or regional economic development programs.

In addition to answering specific questions, studies of these subjects would provide basic information for economic analysis of the priority to be given to research among health activities and of the allocation of priorities for research among the health sciences.

The justification for a PAHO initiative in this field is that the information is urgently needed to ensure the objective and realistic establishment of priorities for health in the framework of the social and economic development programs of the Americas, and that it is not being undertaken under any other auspices. The only study being undertaken at the international level in the Americas at present is an investigation of the economic impact of malaria eradication by the University of Michigan, with technical assistance and supplementary financing provided by PAHO. The Bureau took the

initiative in promoting this project on the basis of Resolution XVI of the XII Meeting of the Directing Council (Havana, 1960). Resolution XXIII of the XII Meeting and Resolution XXIII of the XIII Meeting (Washington, 1961) also instruct the PASB to promote work in the field of health economics.

It is suggested that the Organization begin with a limited number of pilot projects typifying different fields of health economics and promising to yield basic methodological information as well as the answers to specific questions. The following three projects illustrate the kinds of work envisioned.

Study of Cost of Health Services and Medical Care

The problem

Planning for health services in the Americas is handicapped because of the lack of comprehensive measures of the cost of health services and medical care. It is necessary to obtain information on health expenditures of national ministries, social security agencies, and regional and local units of government, as well as data on medical and health services provided to special population groups (the military, plantation workers, schoolchildren, etc.). Quite as important as the aggregate figures are the breakdown into current and capital expenditure and the functional breakdown into expenditures for medical care, preventive services, education, and research.

The method

The World Health Organization recently completed a pilot study of six countries in an attempt to develop definitions and standards in order to establish procedures for collecting data on costs and sources of financing.

The study will be expanded to other countries in 1962 - 1963. PAHO can contribute technical advice for the studies in the American Region, and at the same time the "analysis in depth" of the results would improve the basis for health planning in the framework of the Alliance for Progress. Investigators would visit each national agency known to provide health and medical service, analyze their records so as to obtain comparable information which could be combined to provide global national statistics and, for the private sector, would use survey techniques.

Results to be obtained

A methodology would result that could be progressively extended to other countries on a comparable basis. A full picture of the proportion of national product devoted to health and the proportion of gross capital formation representing investment in health facilities would be obtained. Comparisons with basic economic statistics (wages, consumer income, tax revenues, government borrowing) would clarify the functional relationship between economic levels and the amounts and kinds of health services utilized in American countries.

Study of the Beneficiaries of Health Services

The problem

Much of the planning for the extension of health and medical services in the Americas is undertaken without full knowledge of the potential beneficiaries. Who and how many need the services? What benefits will they obtain? What alternatives exist for them?

The method

Using pilot areas with well-developed integrated health service projects, sample survey techniques would be used to classify persons attending out-patient clinics, hospitalized, and otherwise benefiting from the health services by place of residence, labor force status, and occupation as well as by the conventional demographic indicators. A random sample of the inhabitants of the estimated service area would be classified by the same characteristics, by use or non-use of the health services provided, and by availability and utilization of alternative sources of health care such as clinics, hospitals, private physicians, practitioners of folk medicine, and self-medication.

Results to be obtained

Data for use in comparing costs and benefits would be made available. The economic evaluation of the role of integrated health services in satisfying health needs and effective demand (i.e., what people want and are willing to pay for, as distinct from what they need) would be facilitated. Guidelines for the internal organization of integrated health services would be made available.

Study of Health Needs of Economic Development Regions

The problem

In planning for social and economic development in the Americas, even when health is taken implicitly into account, an additional precise quantitative appraisal of the health requirements created by specific develop-

ment projects, and of the way in which specific health services can potentiate economic development, is needed to guide planning.

The method

Research would be undertaken in a major development area such as the Northeast of Brazil where a national economic development agency is already operative. The economic plans would be analyzed and projections of health requirements would be made (1) at the local level for specific agricultural or industrial development projects and (2) on an aggregative basis for the development region as a whole. Surveys would be made by social scientists of the health and health care status of families, and specialists would study vector-borne diseases, zoonoses, and the environmental sanitation problems created by new urbanization and by rural development schemes. The health information would then be related to the manpower requirements of the development projects.

Results to be obtained

The study of health conditions and the manpower requirements of the development projects would lead to a series of projections of the kinds of health work that would be needed to implement the economic activities foreseen. Precise quantitative estimates would be made available of the medical and paramedical personnel and of the investment in health facilities required. These in turn would serve as a guide to economic development planners and to the officials concerned with planning health services and training health personnel. A general methodology would be formulated which could be applied at the local and regional level in other development areas and lead to the development of a national planning technique.

One of the most important contributions of health economics cannot be formulated in terms of specific research projects - this is the role of health economics as a supporting service in the design and execution of research projects in other fields. Examples are the role of agricultural economics (e.g., farm management, marketing and commodity distribution) in research in applied nutrition and the use of linear programming and other econometric techniques in research on public health administration and the organization of health services. Joining forces with the other health professions, the health economist can add an economic dimension to work in their special fields of interest. Health economists, consulted at the planning stage, can also provide an interdisciplinary approach in the formulation and, when necessary, in the execution of biomedical research.

RESEARCH NEEDS IN MEDICAL CARE IN LATIN AMERICA*

At the beginning of March the Pan American Health Organization called a meeting in Washington of a Special Advisory Group on Medical Care. Recommendations of this Group included systematic research into the administrative principles of medical care - organization and administration of equipment, personnel, and services - and the practical application of the findings for their better distribution, improved efficiency, and lower costs. It was considered imperative to emphasize research in the administrative field, rather than in biological or clinical fields which at present are more widely understood and supported. Also it was considered indispensable to obtain reliable data on personnel, equipment, organization and utilization of services, and especially all aspects of financing. These data are needed for the establishment of a basic organization structure with a very precise objective. Definitions and indices should be established. There was agreement on the utility of certain procedures (morbidity studies in particular) and on the importance of distinguishing between data obtained in special studies and those that should form part of routine collection.

The Group formulated three general recommendations: (a) the establishment in each Ministry of Health of a research unit to collect the basic information to be used for program formulation and continuing evaluation, (b) special studies of those aspects that can best orient medical care administration, and (c) the development of pilot projects to serve as a basis for various schemes of organization, integration of preventive and curative action, regionalization, organization of services, and best use of personnel.

*From RES 1/17 prepared by the Regional Advisor in Medical Care, PASB.

As a working hypothesis, the following subjects can be considered basic for an applied research program in medical care. The proposed subjects appropriately comprehend the four avenues by which the solution to any health or other problem is reached: (a) programming, (b) organization and administration, (c) personnel, and (d) research. There are others, however, whose urgency and usefulness need no further discussion: (e) collection of the basic information indispensable for rational medical care planning, (f) organization and improvement of medical care statistics, (g) regionalization and integration of services and improvement of home and outpatient care, (h) education and training of personnel, and (i) creation and strengthening of applied research agencies.

The foregoing ideas on programming indicate the multiplicity of activities that would be required to put medical care on the road to success so far as direction, management, provision, and application are concerned. The following are some of the questions that must be answered:

How to collect the basic information necessary for consistent planning of medical care? How shall health care activities be organized and administered to establish the link between public health services and medical care within a balanced and harmonious system? How are the appropriate areas of experiementation and in-service training to be determined? How can the schools and other teaching institutions be brought to give the proper orientation during the training of medical care personnel especially those at the higher levels? How shall applied research be conceived, directed, and performed? How, finally, can these activities be carried on simultaneously in such a way that none will suffer?

The problem is unquestionably a complex one and its solution will require concerted action. There has been some thought of promoting basic medical care service in practice, but without deviating from the principle of integration that will lead to an appropriate and progressive solution.

Once the function has been defined, the four approaches determined and the feasibility of the idea accepted, the next step is to create the structure - within a single organization or a diversified one, national or international - and to carry out the research in fields of greatest interest. For this, it is necessary to have adequate financing, bilateral or multilateral assistance, and the sponsorship of a medical school and of a school of public health that wish to discontinue making the futile distinction between public health administration and medical care administration.

Experience shows that other regional or inter-country institutions and centers have been effective in approaching solutions to such diverse problems as nutrition, the zoonoses, and mortality statistics. Considering how large medical care looms in any national budget, the effort assumes the proportions of a highly productive investment.

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