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PROSPECTS FOR INVESTIGATIONS OF VIRAL RESPIRATORY ILLNESSES IN LATIN AMERICA

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PROSPECTS FOR INVESTIGATIONS OF VIRAL RESPIRATORY ILLNESSES IN LATIN AMERICA*

Introduction

The acute respiratory illnesses are one of the most common causes of morbidity in man. These illnesses tend to be most severe among infants and children who are experiencing first infection and among the aged and the debilitated. In these people, the clinical consequence of infection is quite significant and sometimes results in death. In the majority of the population, however, the illness is mild and is likely to be regarded more as a nuisance than as a threat. The consequence of respiratory illness is usually measured, therefore, in the socio-economic sense in time loss from productive effort, in loss of efficiency, and in cost for medical care.

The great importance of the respiratory illnesses from the standpoint of human well-being and in relation to loss of productive capacity has provided both the stimulus and the justification for an expenditure of maximal time and effort toward studies to elucidate the etiology of these diseases and to bring them under control.

It may be expected that eventually, a significant portion of viral respiratory illness will be amenable to prevention by immunization procedures. Development of such procedures must of necessity, however, follow three basic steps:

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*Prepared for the Second Meeting of the PAHO Advisory Committee on Medical Research, 17-21 1963, by Dr. M. R. Hilleman, Director, Merck Institute for Therapeutic Research with the collaboration of Dr. E. H. Lennette, State of California Department of Public Health, both acting as Consultants to PAHO.

a) First, the discovery of the etiologic agents and the definitive establishment of their causal relationship to human illness.

b) Second, the assessment of the importance of each virus with respect to attack rates for infection and to an appraisal of the clinical consequence of such infection especially with regard to the seriousness of the disease and to the degree of debility rendered.

c) Third, the development of potent vaccines employing those viruses proved important from the clinical and public health standpoints, followed by proof of efficacy of vaccines under actual field conditions.

Most simply stated, we must learn what viruses are causing how much of what sort of illness so that one can develop vaccines or other effective control measures against those particular agents which are of public health importance. Non-specific epidemiologic or environmental measures have shown little promise for effective control of any but a very few of the respiratory viruses. The real prospect for significant progress in this area is by artificial immunization approaches and there seems little purpose for detailed studies in viral respiratory disease causation unless the ultimate intent be one of development of technology for effective control.

The following technical reports provide a comprehensive background of the world situation and give recommendations for respiratory

disease investigations on a world-wide basis.

a) World Health Organization Technical Report Series, No. 64, Expert Committee on Influenza, First Report, April 1953.

b) World Health Organization, Technical Report Series, No. 170, Expert Committee on Respiratory Virus Diseases, First Report, 1959.

Acknowledgment: In making this report, both site visitors wish to acknowledge and to express their sincere appreciation to the many Latin American scientists who gave most excellent cooperation and enthusiastic reception in this endeavor.

Present Knowledge and Unsolved Problems

The first half of the present century saw little progress in the definition of etiology in respiratory disease and in development of methods of control other than for influenza A and B, Q fever and the psittacosis agents. The introduction of modern tissue culture methodology in the early 1950's has since led to the definition of a large number of respiratory virus families and of individual respiratory viruses.

A list of the presently known respiratory viruses is presented in Table I, page 5.

It is undoubtedly true that many serologic types belonging to the discovered families of respiratory viruses remain to be found. It seems possible and probable also that as yet undiscovered families

of viruses causing respiratory illnesses are still to be found.

Programs conducted principally in the U.S.A. and in Europe have started to define the relative importance of several of the known respiratory viruses in acute respiratory illnesses of man. Assessment, to date, cannot be made in terms of agent-specific attack rates for each virus. Instead, this can only be made with reference to per cent contribution of each agent to the total of respiratory illness in a given population. Such assessment of relative importance of a particular respiratory virus in total respiratory disease must, of course, be made according to age group and it must take cognizance of the clinical consequence of the infection, i.e., severe (hospital cases) vs. mild (outpatient cases) illness. True appraisal of overall importance can only be made in terms of proper selection of cases at large in open non-institutional settings. Closed population groups generally present abnormally frequent epidemic occurrences of viral infections and hence do not reflect the true picture in the population at large.

One such assessment of relative importance of viruses is pictured graphically in Figure 1. It depicts the per cent contribution in children vs. adults, and in severe (hospital) vs. mild (outpatient) illnesses of each of a selected group of respiratory disease agents. (The bases for the conclusions are to be found in the following references: Hilleman, M.R., et al., Acute Respiratory Illnesses Among Children and Adults, Field Study of Contemporary Importance of Several Viruses and Appraisal of the Literature. JAMA 180: 445-453, 5/12/62; Hilleman, M.R., Respiratory Viruses and Respiratory Virus Vaccines. Am. Rev. Resp. Dis. 87: 165-180, February 1963). The outstanding

TABLE I

KNOWN RESPIRATORY VIRUSES OF MAN

Myxovirus influenza, types A,B,C
Myxovirus parainfluenza, types 1, 2, 3, 4
Myxovirus (?) respiratory syncytial virus

Adenovirus, more than 28 types

Enterovirus
- ECHO viruses, at least 30 types
- Coxsackie A, 24 types
- Coxsackie B, 6 types
- Poliovirus, 3 types

ECHO 28-rhinovirus-coryzavirus group (ERC), $\geq$ 27 types

Reovirus, 3 types

Mycoplasma (Eaton agent - pleuropneumonia). Cold agglutinin positive atypical pneumonia

Psittacosis-ornithosis (bird contact)

Miscellaneous
- Lymphocytic choriomeningitis
- Infectious mononucleosis
- Measles (giant cell pneumonia)
- Q fever
- Other

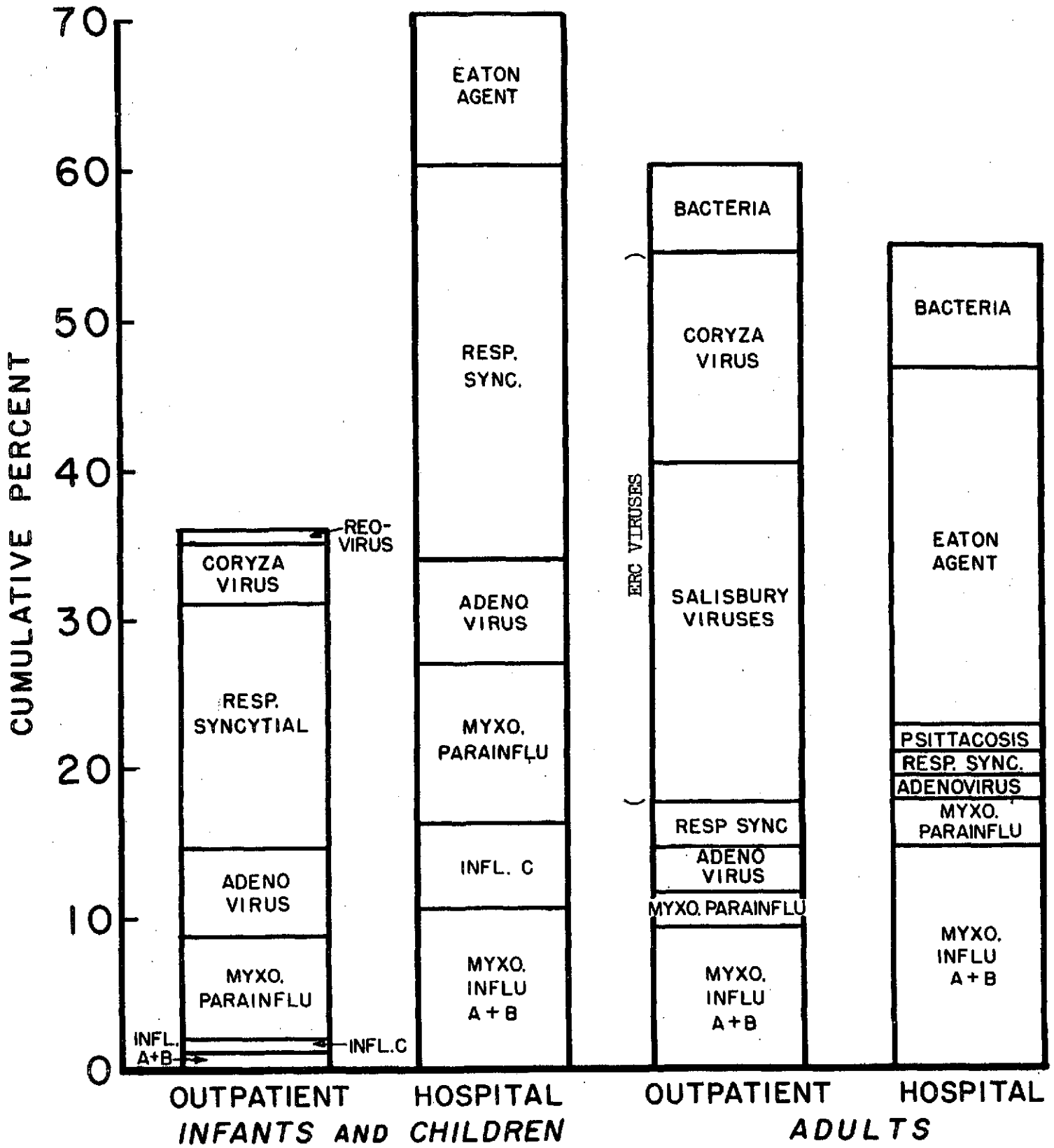

FIG. 1. OVERALL ESTIMATE OF RELATIVE IMPORTANCE OF RESPIRATORY DISEASE AGENTS, ACCORDING TO AGE AND TO CASE SELECTION.

points are (1) the relative importance of each agent with respect to its contribution to respiratory illness and (2) the difference in relative contribution of each virus in adult vs. child respiratory disease and in severe vs. mild illness. Appraisals such as this provide the background knowledge necessary for intelligent selection of virus candidates for viral vaccines.

Pertinent information has been gathered also as to the epidemic or endemic patterns of occurrence of several respiratory viruses in non-institutional open populations. Influenza A and B, and, interestingly, respiratory syncytial virus infections tend to occur in cyclic epidemic waves. The remaining agents, except for unusual associations among individuals (e.g. orphanages, military camps, boarding schools), tend to occur more in an endemic or perhaps "constantly epidemic" pattern.

Certain of the viruses, specifically influenza A and B, show a constant and progressive change in pattern of antigenic composition which seems to be the combined result of developing herd immunity and selection of antigenic variants. Such variation seems requisite to virus survival. Most outstanding in such variation is the very marked or abrupt change which seems to occur at perhaps 10 or more year intervals, usually at a time when herd immunity has fairly well caught up with ordinary strain variation. The source for such abrupt change might be from a mutational origin or possible release from an animal host reservoir. It is a subject of much importance and one on which information is being gathered in the contemporary period.

Attempts to define the precise clinical course and the total clinical spectrum for each of the known respiratory viruses have been only partially achieved. Knowledge also pertaining to gross and micro-pathology in fatal human cases of respiratory illnesses, according to specific etiology, is presently lacking for most of the respiratory viruses.

Present Knowledge and Activity as it Relates to Latin America

Epidemiology-Statistics

Extensive review of the literature (confirmed by the site visits) has revealed an extreme paucity of knowledge relating to epidemic or endemic occurrence of acute respiratory illnesses in Latin America. Such significant information as is available relates primarily to the 1957 pandemic of Asian influenza. Chile, perhaps, has the most extensive information relating to respiratory disease. In Chile, with a population of 8,000,000 persons, there are 18,000 deaths per year from respiratory disease. Twenty per cent of all deaths are of respiratory origin. Respiratory disease ranks first as the cause of death in Chile and these fatalities occur mainly in the very young and very old. Such figures certainly attest to the importance of respiratory disease as an important health problem in Latin America as in the rest of the world, although the figures for Chile may be out of proportion with the general Latin American experience Certain important epidemiologic and statistical information may lie buried in the records of various institutions - Dr. Nogueira, e.g., in São Paulo has extensive information concerning respiratory illness as a cause for absenteeism among workers in the textile industry.

Respiratory Virus Laboratories

Studies of respiratory viruses are very much neglected or otherwise underdeveloped in Latin America. Very few workers would consider themselves as primarily respiratory disease virologists. Instead they do very limited work on respiratory virus diseases often as only a part-time activity of a part-time job, and with intent only to provide a limited diagnostic facility. Their physical facilities are mostly poor in terms of adequate equipment, although there are exceptions, and their capability to do diagnosis is generally limited to influenza, sometimes adenovirus, and infrequently one or two other agents. They lack an available supply of monkeys to prepare monkey renal cell cultures and have neither reference viruses nor reference antisera to permit an expanded activity into studies of additional agents.

These observations are in no way intended as criticism - they merely reflect the stage of development of the activity. There has been no intensive stimulation of this area of research in the past and adequate numbers of highly trained personnel are generally not presently available to carry it out - training is needed.

Clinical Activities

The clinical aspect relating to studies of respiratory illnesses is certainly adequate from routine clinical practice in out-patient clinics, hospitals, dispensaries, etc. There is wealth of clinical material available and this needs only to be tapped.

A General Plan for Studies of Acute Respiratory Illnesses in Latin America

It is clear that many competent investigators would pursue a viral respiratory disease program with enthusiasm and vigor if only the necessities were made available to them.

By simplest definition, these needs could be met by training and money. The balance of this report deals with what might be done in the specific sense.

Epidemiology

The ideal ultimate overall objective in assessing respiratory disease importance would be to obtain statistics for morbidity and mortality according to age, season, geography, social or occupational situation, etc. Additionally, special studies of the precise patterns in epidemic occurrences should be sought.

Such ideals have been only partially and superficially achieved, even in the U.S. There are, however, existing sources of information in Latin America which might be very useful if only utilized. City, state, and national mortality figures for respiratory disease are sometimes available. Hospital and clinic admission information can be utilized. School, industry, government and other absenteeism records are sometimes kept on a disease category basis. These ought to be gleaned for purpose of informational summary and

appraisal. Better statistical reporting should be sought - perhaps with household survey sampling if such could be developed.

Appraisal of Respiratory Disease on an Agent-specific Basis

Clinical

Clinical sites for random selection of cases need to be established. These may include pediatric outpatient clinics, hospitals, factory, school or college dispensaries and the like. At the time of the initial patient's visit a history plus a sample of throat secretions (in veal broth) and a sample of blood are taken. Another blood and follow-up case history are taken 3 weeks later. Respiratory secretions are stored frozen at -70ºC (either in a mechanical refrigerator or in sealed glass vials in dry ice), and the sera are stored at-20ºC until tested. A control group of cases should also be selected on an equivalent basis from non-respiratory cases to assess the significance of positive results among the cases of respiratory disease. Serologic findings among hospital cases may be misleading owing to intercurrent infections picked up from other patients in the hospital during the 3 week interim between collection of blood samples. For such specific purpose, virus isolation results are more reliable.

Special studies of post-mortem cases may be of extreme importance in establishing cause of death and pathologic descriptions of respiratory disease on a virus-specific basis. For such studies, cases of early death would be most desired and virus recovery from aseptic autopsy specimens would be needed for etiologic diagnosis.

Laboratory

The laboratory should be equipped to handle both virus recovery and serologic diagnoses. Except for special studies of cases in the hospital or for other intended purpose, serologic diagnoses for most viruses are far easier to accomplish and are generally more sensitive than by recovery and identification of the causal agent. For diseases caused by viruses of multiple serologic type and for which no generic or group-specific test is available, as for enteroviruses and ERC agents, then virus recovery may be the only practicable method to use.

Certain of the diagnostic tests are far more difficult to render than are others and there may be advantage in concentrating initially on a single family or group of viruses rather than in attempting to cover a sizeable portion of the spectrum. For starting purpose, influenza A2 and B2, parainfluenza 1, 2, 3, reovirus group, adenovirus group, respiratory syncytial, and Eaton agent (cold agglutinin positive PAP) diagnoses might be rendered on a serologic basis. Later, with development of serologic typing reagents, virus recovery and type-specific diagnoses for these agents plus enteroviruses and ERC agents might be rendered.

Virus recovery and serologic typing of influenza virus strains are always of special importance in keeping influenza virus under close surveillance so as to apprehend significant antigenic changes before they assume nationwide or worldwide importance.

Once a general appraisal has been made of which of the known viruses are causing respiratory disease and how much and what sort of illness, then the still undiagnosed cases become of paramount importance. These undiagnosed case samples become the point of major attack in the search for agents as yet undiscovered.

For purpose of preparing diagnostic antigens for, e.g. CF tests, and for making positive control or typing antisera, it is necessary to obtain and maintain a museum of known respiratory disease agents. It would be far better to obtain the reagents themselves from commercial or governmental sources. Unfortunately such are generally not available at present and each laboratory must resort to making its own. For this purpose, seed strains and reference antisera are necessary.

For conduct of laboratory investigations along these lines, a reliable and significant tissue culture producing laboratory is essential. For preparing antigens (for serology and animal immunization) and for virus recovery and identification purpose, each laboratory should have available cultures of primary monkey kidney (South American monkeys ought to be explored for utility), one or two human cell lines (HeLa, KB, HepII) and a human fetal cell strain such as WI-26 or WI-38. Perhaps the BSC-1 Cercopithecus monkey kidney cell line could substitute for primary monkey renal cell cultures.

Proper equipment for low temperature storage is essential to accomplish these objectives.

For conduct of serologic tests, use of micro-equipment which permits use of micro amounts of specialized reagents should be fostered (See: Sever, J.L., J. Immunol. 88:320, March 1962). Availability of reagents is a major issue and conservative use of such materials is of extreme importance.

Personnel

For an active, large-scale study, the following numbers and kinds of persons would be needed. Useful information may, however, derive from more modest outlay.

a) Clinical

Two or three half-time or two full-time physicians for clinical case sampling.

One full-time nurse.

b) Laboratory

Tissue culture production crew- three or four persons, including one highly competent technical chief.

Virology:

One chief of laboratory - preferably M.D. or Ph.D. level.

Four or five B.S. equivalent technicians.

Dieners as needed.

c) Epidemiology

One epidemiologist - desirable for gathering general statistics, guiding case sampling, etc.

d) Secretary

At least one with primary function of keeping records and getting patients back.

Recommended PAHO Activities

Philosophy

It is believed that the Pan American Health Organization should make every effort to assist interested Latin American investigators in establishing programs for study of viral respiratory disease. Such assistance includes funding, personnel training and technical assistance, supplying basic needs for specialized reagents, and providing technical information.

As a basic philosophy, it seems more important to obtain earnest initial starts with gradual expansion than with pretentious large-scale planning which is unlikely of accomplishment. The laboratory diagnosis of viral diseases, at best is difficult, and successful accomplishment is more in the nature of a research achievement than in the fulfillment of a routine procedure. The accomplishment of even a modest number of diagnoses in Latin America is an important accomplishment in beginning to furnish knowledge of respiratory disease causation where so little is presently known. It would seem important that this philosophy and concept be clearly imparted to granting agencies which might be asked to furnish funds for investigations in Latin America.

Further to this, it will be necessary for granting agencies to accept the facts of life as they are in Latin America, e.g., instability in administration of certain institutions, non-availability of highly trained personnel in many instances, and half-time or only part-time participation on the part of principal investigators. These are matters not readily subject to change. It is expedient to provide an incentive

for research and to accept what can come of it within the limits of what is presently practicable and possible.

Most important is the need to provide means for upgrading or supplementing salaries for workers. This must be accepted as a basic essential to any program if the capable people are to be attracted to and kept in such research activity.

Funding.

It is believed that research support might well be of two sorts.

1. Individual investigators with amply trained staff and appropriate facilities might well be encouraged to make proposals for research on a wholly independent basis. PAHO should assist in obtaining and preparing application forms and should be helpful in advising interested Latin American investigators of sources from which economic assistance can be obtained. Support should also be given to investigators by contacting the administrations of their individual institutions and advising them of the need for a strong and long-term commitment to work on these problems. Stability for the investigator seems essential.
2. PAHO might, itself, seek funds for minor support to small-scale projects which represent no more than making a basic start in the field, preparatory perhaps to expansion at a later date. Such funds could take care of

certain essential needs which would make the difference between a program and no program.

It seems senseless in this report to endeavor to point out individual program needs. Programs must be generated locally and each prospective investigator must state his need as he best sees it. Support in the range of $10,000 to $40,000 per year per investigator would not appear unreasonable.

Training.

Funds should be sought to permit principal investigators to spend a year or two in the United States or in Europe, perhaps, for advanced basic training.

More important is the seeking out of means and of trained qualified persons (M.D. or Ph.D. expert in the field) to go to Latin America and actually spend two or three years in a particular institution. While there, the trainer would teach personnel, develop facilities, and establish an active and productive working team and program which would continue after his departure. In such activity, the trainer would best serve only as technical advisor with the Latin Americans in full administrative and organizational control. This seems the only means for building permanence. The request for such technical persons from the outside was almost universally voiced among the local investigators who were visited.

More virus training such as being given by Dr. H. Doany,*

*Deceased since visit.

PAHO consultant in virology assigned to the Oswaldo Cruz Institute in Rio de Janeiro, seems indicated. Funds for travel and maintenance of qualified trainees at such training centers should be sought and provided.

Most Latin American countries have no graduate training program in microbiology equivalent to the Ph.D. This seems a necessary must if the allied and basic medical sciences are to develop maximal numbers of competent persons for contemporary and long-time conduct of laboratory research programs.

Travel funds appear to be mostly non-available even for qualified Latin American persons to attend national or international meetings at which they might improve their knowledge and perspective. PAHO, perhaps, could obtain and administer some sort of travel funds for this purpose.

Reagents and Technical Information.

Non-availability of viruses, reference antisera, antigens and the like provide a formidable roadblock to even the starting respiratory research program in Latin America. Here is an area in which PAHO could be of inestimable help. Funds should be made available for obtaining and for sending selected virus respiratory disease agents to interested Latin American investigators. Essentially all of these agents are obtainable from the American Type Culture Collection in Washington, D.C.

Reference reagents are being prepared in the contemporary period by contracts from the National Institutes of Health to commercial sources and by the grants mechanism. While these reagents are intended primarily for use by grantees, PAHO should explore with the National Institutes of Health the availability of these materials for use by qualified investigators in Latin America.

Technics for preparing routine diagnostic and typing reagents are difficult to assemble, especially where library facilities may not be complete. It may be of great assistance to Latin American workers for PAHO to seek to obtain from NIH and to furnish to them the detailed methods for reagent preparation as outlined by the NIH Panel for Respiratory and Related Viruses. These would serve as a most helpful guideline for the investigator who is faced with the problem of making reagents for the first time. Reprints or photostatic reproductions of pertinent important articles on respiratory virus investigations as they appear might well be provided by PAHO to qualified investigators in Latin America on a selected basis. One complaint often heard was that journals are so late in arriving and often so hard to get hold of that the most recent literature is of essentially no help in assisting contemporary work.

Respiratory Disease Study Centers.

Presently, there is no single laboratory which could function effectively in this capacity. This seems a basic necessity in the longer term but can only develop from the modest beginnings which can be made at present.

It seems worthy of emphasis that it is important to get work started, no matter how modest. From such beginnings may develop large and highly effective programs.

PAHO Research Coordination.

It would seem essential for PAHO to keep abreast of all developments and to take care of needs and promote research on an international basis. Biannual reports by the investigators for purpose of advice and orientation would seem of inestimable help to PAHO in fulfilling its stated mission of research aid and coordination.

SUMMARY OF FINDINGS IN SITE VISITS*

I. Brazil

A. (3/25/63) Institute of Microbiology
University of Brazil
Avenida Pasteur 250, Rio de Janeiro, Brazil
Director: Dr. Paulo de Gôes

Division of General Microbiology. Dr. Amadeu Cury, Head (also Asst. Dir. of Inst.)
Division of Virology. Dr. Manuel Bruno-Lobo, Head.

1. Activities.

Research. The Divisions of General Microbiology, Virology, Immunology and Medical Microbiology are devoted to research activity.

Research in virology began about 1950 with special emphasis on the neurotropic viruses. Principal activity was centered from 1951-1956 on enteroviruses including Coxsackie and polio viruses. The program was largely diagnostic but included work on definition of clinical syndromes associated with Coxsackie infections, sero-epidemiology, and animal pathology.

During 1957, very extensive investigations were made of Asian influenza in Rio in the virus diagnostic sense, in sero-epidemiology, and in studies of antigenic pattern. Some of this work has continued to the present.

Work on arboviruses was started in 1958. Studies of

*Dr. M.R. Hilleman made site visits in Brazil, Uruguary, Argentina and Chile. Dr. E.H. Lennette made site visits to Mexico, Costa Rica, Panama and Venezuela

possible antigenic heterogeneity in yellow fever strains and of serologic responses to yellow fever vaccines were made. A serologic survey in Rio was carried out with special emphasis on EEE and WEE. Animal pathologic response to equine encephalomyelitis viruses was studied. This laboratory cooperates with the Evandro Chagas Institute in Belém.

Present work includes studies to recover adenoviruses from tonsils and adenoids from adults and children in Rio. This program was started by Dr. H.G. Pereira (London). A number of strains (57) have been isolated and identified. Dr. de Góes has influenza, parainfluenza and adenovirus strains and antisera.

Dr. de Góes has a functioning tissue culture laboratory.

Training. This is a training center in microbiology, virology and immunology for all of Brazil, with emphasis on training for teaching and research. Students are recruited from among advanced students and faculty of the schools of human and veterinary medicine, dentistry, pharmacy, etc. Dr. de Góes has trained more than 300 microbiologists for Brazil. There are about 12 students received per year.

Service. Not a service organization.

2. Resources.

Physical. The Institute is housed in a new and an old

building (combined). One small suite of laboratories in the old building is available for virus research activity. This suite, which includes areas for tissue culture, animals, serology and virus work, is adequate to handle a single virus program but could not do more, efficiently. It would be quite adequate for a program in respiratory disease but should not include other programs except on an emergency basis.

Equipment. The laboratory is moderately well equipped but could do well to be modernized with new sterilizing equipment, dry iceboxes, a standby generator and the like.

Personnel. Dr. de Góes presently has 2 technical people available for this work. These are Dr. J. Ciribelli Guimarães and Dr. R. D. Machado, both of whom were trained by Dr. Pereira. They have the equivalent, perhaps, of 1 year beyond the B.S. plus experience.

For a good respiratory study, many more people would be needed. The big problem in Brazil is to upgrade salaries so as to attract and hold reliable people. This can best be handled at present by salary supplement from an outside source.

Dr. de Góes can recruit all the people he would need for the program for the routine work including physicians, nurses, epidemiologists, laboratory people, etc.

The real need, however, is for a well-trained person from

the outside, perhaps PAHO, Europe, or U.S.A. to spend one to 3 years helping out in training and getting all the technology established. Dr. de Góes would have funds to pay such a person up to $13,000/yr., plus travel, from his own Ford Foundation grant and from the overall grant to the university.

Funds. Dr. de Góes receives regular support from the university. He also receives the following funds from Ford Foundation (1962, $37,000; 1963, $12,000; 1964, $12,000) for visiting professors. The university has $120,000 of such similar funds for the whole institution. None has been earmarked and some of this also would be available to Dr. de Góes to bring in one or more highly trained person from the outside to help in getting a good program going.

Connections. Dr. de Góes has an excellent working relationship with all the principal hospitals in Rio de Janeiro. Patients for clinical observation and as a source for paired blood samples should be available and cooperative. Epidemiologic information to appraise incidence of respiratory disease according to age and season can likely be obtained from absenteeism records of schools and factories. More elegant and refined methods might be developed later.

3. General plan and appraisal.

Dr. de Góes expressed great interest and enthusiasm in

conducting studies in viral respiratory disease. It is believed that Dr. de Góes is capable of carrying out a good respiratory virology program. He has a reputation for energy, organization and proper connections. Four elements seem essential to success, however. These are:

a) Funds to upgrade equipment, purchase dry ice, etc.

b) Attention to a single problem, respiratory disease, except for temporary emergency need. (Duplication of activity seems unnecessary. Arbovirus work is covered at Belêm and enterovirus at the Oswaldo Cruz Institute).

c) Funds to hire needed additional personnel and to supplement basic salaries.

d) Bringing in one or two well-trained persons from the outside who are thoroughly knowledgeable in virus and cell culture technology (preferably in respiratory virology) for 2 or 3 years.

To get started, possibly Dr. Hanna Doany, WHO consultant from the Oswaldo Cruz Institute, could help in this for 2 days per week.

A reasonable request from Dr. de Góes might well include funds for equipment and supplies (dry iceboxes, dry ice, glassware washing, incubator and the like).

Personnel (2 halftime M.D.'s for specimen and history taking; 1 epidemiologist; 2 halftime nurses; 3 technicians; 2 dieners; 2 laboratory scientists (Drs.); other?).

It may be emphasized that it would seem far more important to bring in one or two consultants from without to train the respiratory research staff on site than to send a person off somewhere else for training. The man from without could not only upgrade the training of the entire assembled staff but could also help in implementing a working program.

B. (3/25/63) Instituto Oswaldo Cruz (Central Brazilian Govt. Lab.)
State of Guanabara
Caixa Postal 926
Rio de Janeiro, Brazil

Director: Dr. Joaquim Travassos
Asst. Director: Dr. Areia Leão

Dr. Laura Maria F. Queiroga - In charge of Enterovirus Laboratory
Dr. José Guilherme Lacorte - Director of Respiratory Virus Research Section, Director of the WHO Influenza Collaborating Laboratory.
WHO/TA: Dr. Hanna Doany, Virology Consultant

1. Activities.

This is the central Brazilian government laboratory. It is a large institution and has many activities.

Research work in arbovirus is carried out in connection with the Evandro Chagas Institute and with the Virus Laboratory in Belém.

Dr. Queiroga, with the assistance of Dr. Hanna Doany, carries out an extensive enterovirus research activity. They have an excellent tissue culture activity, complete with human cell lines developed at their laboratory. They carry out diagnostic tests for the whole of Brazil and provide

reference antisera to other laboratories. This laboratory is presently carrying out control tests of imported Sabin live poliovaccine.

Each year Dr. Doany conducts a 6 week course in cell culture technology and virology. This is attended by trainees from all over Brazil.

2. Resources.

The virus laboratory of the Oswaldo Cruz Institute is spacious and well equipped.

3. Possible respiratory project at Oswaldo Cruz Institute.

Dr. Doany will probably remain at the Institute for the next 2 years. During his tenure, the Institute would be in a good position to undertake a program of study in viral respiratory disease.

Dr. Travassos seemed eager to have such a study going at the Institute and is willing to turn over a spacious suite of presently empty rooms to such a venture. He stated his willingness also to convert these rooms to working virus laboratories which could be ready for operation within 3 months' time.

Setting up a program at Oswaldo Cruz would entail most of the problems and special needs described above in connection with Dr. de Góes' study. In all of these, support for salaries to provide for quality permanent staff is all important.

The undertaking of a respiratory study at Oswaldo Cruz ought to depend upon some firm commitment on the part of the government to lend support to the program for at least 5 years. Additionally, it would require some commitment on the part of PAHO/WHO to have Dr. Doany or his successor actively help in establishing and in operating the program. A clinical field operation would have to be sought and established by the Institute to provide specimens. This should be possible.

C. (3/26-27-63) Adolfo Lutz Institute
Avenida Dr. Arnaldo 3
C.P. 7027
São Paulo, SP, Brazil

Director of Institute: Dr. Ariosto Büller Souto
Director, Division of Microbiology & Diagnostics: Dr.Luis de Salles Gomes
Director, Virus Section & Laboratory of Pneumotropic Viruses: Dr.Luis A. Ribeiro do Valle
Dr. Arno Ruy Fisher is in charge of the Pneumotropic Virus Laboratory.

1. Activities.

Research. This is the public health laboratory for the state of São Paulo. Dr. Ribeiro do Valle's laboratory has been engaged in virus respiratory work since 1953. Laboratory proof of occurrence of influenza was obtained in 1953, 1957, 1958, 1960, 1961 and 1962. This is a designated influenza laboratory of the World Health Organization. Serologic tests of adenovirus cases are now being carried out and attempts at isolation of adenoviruses from human tonsils and adenoids are being made. Specific etiologic

diagnoses have recently been rendered in cases of atypical pneumonia caused by psittacosis, Q fever, or influenza. The Institute has a good producing tissue culture laboratory. It would need to be upgraded with addition of cell lines such as BSC cercopithecus kidney and human cell strain WI-26.

Training. Not a training center.

Service. Virus diagnostic activity for the state of São Paulo.

2. Resources.

Physical. Dr. Ribeiro do Valle has a most excellent and adequate physical plant to carry out a respiratory research program. The laboratories are relatively new, well-constructed and would be considered very good by U.S. standards. Animal quarters are quite adequate. The cell culture organization is functioning. There are plenty of sterile rooms.

Equipment. The laboratories are very well equipped and would need only minor additions. Adequate supplies of dry ice might seem desirable.

Personnel. Dr. Ribeiro do Valle has had experience with viruses and rickettsia since 1944. He trained for one year (1944) at the Hooper Foundation in San Francisco. He worked in diagnosis of influenza, psittacosis, ornithosis, Q fever and poliomyelitis during the next 3 years at the Institute Butantan and at the Institute Adolfo Lutz. During 1947/48, Dr. Ribeiro do Valle spent a year in the Department of

Bacteriology, University of Liverpool (England) and in the Department of Bacteriology of London Hospital. Dr. Ribeiro do Valle works half time at the Institute and half time at a private laboratory which he operates. He has 4 hours per day to devote to respiratory disease research.

Dr. Arno Ruy Fisher is in charge of the pneumotropic virus laboratory of the virus section. He has had 4 years of experience in microbiology, the last 3 years being devoted to virology. His principal experience has been concerned with adenoviruses, influenza viruses and cell culture. Dr. Fisher is also an instructor in the Department of Microbiology at the Paulista School of Medicine in São Paulo.

Trained technicians are presently on hand. Dora de Almeida Padilha has had ten years' virus diagnostic (isolation and serology) experience. Durval Zagnetti has had 2 1/2 years' experience along similar lines.

Funds. Dr. Ribeiro do Valle is supported by the Institute. He would, however, need additional funds to upgrade salaries and to put his people on a full time basis. He would likely need some equipment. Dr. Ribeiro do Valle would certainly need a full time M.D. or 2 half time M.D.'s to participate in the clinical work plus a nurse. An epidemiologist might be added on a part time basis.

Connections. Dr. Ribeiro do Valle has excellent connections with the Pediatric Department of the School of Medicine of the University of São Paulo. Dr. Aeddo de Oliveira, assistant professor, is in charge of the clinics. Two capable

residents, Dr. C. Peteau Trinidadi and Dr. Paulo Bearzoti are available, interested and enthusiastic about the prospects for participating in the clinical part of a respiratory program. Both outpatients and inpatients with respiratory illness are available in a ratio of about 4:1, respectively. Plenty of respiratory cases do occur. Over a 3 year period, 650 pediatric cases of bronchiolitis and 2,337 pediatric cases of bronchopneumonia were admitted. These were under 12 years of age.

Dr. Ribeiro do Valle also has contact with a day nursery for working mothers where children with respiratory illness as it occurs in the general child population would be available for study.

A third very excellent connection is Dr. Diogo Pupo Nogueira, who is plant physician for a large textile industry with 3,000 workers. This industry has a requirement that all workers report all illnesses and it maintains a good plant dispensary. Epidemiologic information and statistics for respiratory disease are almost non-available in South America. Dr. Nogueira has epidemiologic information and statistics on respiratory illness in the factory on an annual basis starting in 1949. (Dr. Nogueira was urged to publish his valuable data and to do it in a journal in English.) Dr. Nogueira noted that 52% of all absences of non-occupational origin are of febrile respiratory nature (not including the common cold). Epidemiologic information and specimens for virus laboratory study would be readily

available, as it pertains to the adult industrial worker. This would provide a most important aspect for any respiratory disease program.

Finally, there are many small field laboratories throughout the state of São Paulo where surveillance is made. These satellite stations could keep an alert and sample cases in any unusual outbreaks which might occur outside the city of São Paulo.

There are good facilities at the Institute for studying the bacteriologic aspect of any respiratory illness. Dr. Salles Gomes is the Director for bacteriology.

Dr. Moura is available for consultation. He is primarily an enterovirologist who spent two years at the Pfizer Labs. in Terre Haute, Indiana, in the United States.

3. General appraisal.

Dr. Ribeiro do Valle certainly has proper interest and enthusiasm to carry out a productive virus respiratory disease program. This is especially evidenced by the great amount of effort he has already put forth in lining up sources for study of cases and for collection of epidemiologic information. He has a well equipped spacious laboratory plus a working cell culture production unit. He would have access to a great wealth of clinical material.

Dr. Ribeiro do Valle's most outstanding need would be for a well-trained virologist from the outside to come in and work for two or three years in upgrading cell culture and in training the technical staff in methods and approaches. This needs to be done on a

basis of giving technical help but the operation must be under the control of the local people so that the organization will remain functioning after the technical adviser leaves.

Dr. Ribeiro do Valle might need some funds for equipment. Mostly, however, he needs funds to pay the added nurses, technicians, etc., and to upgrade the salaries of existing staff, so that he can have them on a permanent full time basis.

Dr. Ribeiro do Valle has stated that he would have 4 hours per day to give to the program. He was serious in this. It is believed that he would exert every effort to turn out good work in this activity. A program, properly supported, should be highly productive.

II. Uruguay

A. (3/27-28/63) Institute of Hygiene
School of Medicine
University of the Republic
Montevideo, Uruguay

Director: Dr. Ciro Peluffo (half time)
Head, Virus Laboratory: Dr. Hector C. Tosi (half time)
Department of Pediatrics, School of Medicine: Dr. Carlos A. Bauza

1. Activities. This institution is under heavy teaching responsibilities and engaged in the production of vaccines and antisera. It has very little research activity in virology. The staff is mostly half-time, holding down a second job in another institution such as in the Municipal Microbiology Laboratory.

Dr. Tosi has done some work with influenza in the way of virus recovery and serodiagnosis of cases. He has also done some work with Dr. Raúl Somma and M. H. Giordano in Coxsackie and poliovirus studies.

Presently, under Dr. Pereira's suggestion, some work is being started to recover and type adenoviruses from tonsils and adenoids of human subjects.

There is also a small tissue culture preparation effort going on. This would be in great need of bolstering in order to give adequate support to a virus research program. A few cell lines are being carried and primary chick embryo cell cultures are being made.

The total experience of the laboratory with respect to virus respiratory research would have to be related or rather small.

2. Resources. An adequate amount of presently unused space would be made available for a virus respiratory research program in the Institute of Hygiene. Some additional basic equipment would be needed and part of the area would need to be revamped to supply sterile rooms for tissue culture and virus work. A new medical school is being built and more ideal space might be provided in the new structure. Clinical specimens can be obtained quite readily from hospital outpatient and inpatient sources. Dr. Herrera Ramos, Professor of Medicine (specialty; degenerative disease) and Dr. Pablo Purriel, Professor of Medicine (specialty:

thorax) expressed great interest in the possibility for a respiratory project and in cooperating in such a study. Clinical and laboratory personnel could be made readily available to the project from new graduates and existing staff, provided that funds can be obtained.

Dr. H.G. Pereira (England) is spending 2 months at the Institute on a training mission during the coming summer.

Dr. Eleulerio Vallone will be sent to take Dr. Doany's virus and cell culture course in Rio de Janeiro in July.

Dr. C. Bauza expressed much interest in taking Dr. Doany's course to gain background in virology, even though he is a pediatrician.

Dr. Raul Somma is scheduled to go to the United States (NIH) to study arboviruses. Drs. M.H. Giordano and Y.C. de Vivas Gurri have had training in tissue culture at the CDC/USPHS in Alabama, Georgia and at the University of Michigan.

3. Possible respiratory project at the Institute of Hygiene.

Drs. Peluffo and Tosi seemed most eager to develop a virus respiratory research program. Certainly, excellent cooperation could be had from the hospitals for collecting specimens and clinical data. The laboratory capacity, however, is very much limited, especially technically. It was agreed by all that a trained person from the outside would be needed for 2 or 3 years to help establish and put into

operation a tissue culture and virus program. Support would be needed to add some essential equipment and to hire the laboratory and clinical workers for a program such as outlined above for Dr. de Góes. Upgrading of salaries seems a most important must to get the people on a full time rather than a part time basis and to provide the incentive to remain in the field. Workers are available to hire. This Institute, having to start with somewhat less than most, might well have a more modest beginning. Viruses and reference reagents would be required.

The essential ingredients for a successful program were present. These were primary interest and enthusiasm.

III. Argentina

A. (3/28-29/63) National Institute of Microbiology
(Formerly Malbran Institute)
Avenida Velez Sarsfield 563
Buenos Aires, Argentina

Director of the Institute: Dr. José Maria de la Barrera (Acting)
Chief, Department of Virology: Dr. Julio G. Barrera Oro.

1. Activities. The overall institution has responsibilities for producing a variety of vaccines, for diagnosis, for training staff from provincial laboratories and in-service training, and for research. The Institute has been very active since 1958 in studies of arboviruses and has been mostly concerned with the Junin virus (probably mite-transmitted) which is the cause of Argentina hemorrhagic

fever of man. Field studies of epidemics and serologic surveys are included in the program.

Dr. Barrera Oro has been very much interested in research in the area of viral respiratory disease. He started a knowledgeable project in 1962 in cooperation with pediatricians of the Hospital Pedro de Elizaldo (Hospital of Pediatrics whose Director is Dr. Robert Ceruti). Detailed clinical studies (history, physical, hematologic, X-ray) were done on 40 patients and specimens for diagnosis were taken (including throat and rectal swabs, urine, acute and convalescent blood samples). For non-technical reasons the isolation specimens were lost but the paired sera were retained and tested for influenza A and B. Dr. Barrera Oro is continuing serologic tests with the 40 paired sera and intends now to study 200 more cases. If all goes well, he will set up a program for sampling of cases during all months of the year. The program has been badly upset by loss of staff and other non-technical problems. This is extremely regrettable since a worthy program had been initiated.

2. Resources.

Physical. The Department of Virology is housed in very ample modern quarters which are excellent for conduct of research in the field of respiratory virus diseases. The Institute has a functional tissue culture supply unit.

Equipment. The Virus laboratory would be considered extremely well equipped when judged by U.S. standards. Just about every major and minor kind of instrument is there, including such things as an analytical ultracentrifuge, electron microscope, radioactive counters, etc. Much of the equipment is non-operational, however, for lack of some small part or other repair or for want of trained operators.

Personnel. Dr. Barrera Oro is highly knowledgeable in the field of virology. He spent 3 years in the States at Dr. Melnick's laboratory at Baylor University. The laboratory had a good many highly trained and competent technicians who were let go owing to contemporary and administrative instability at the Institute. These could be recalled if funds were made available. There is no U.S. equivalent Ph.D. training program in Argentina in the field of microbiology. Hence, the people have to be handtrained beyond the college degree. The staff at the Institute is full-time.

Funds. The Institute is amply supported in normal times. However, owing to political unrest and to uncertainties as to the future, many cuts in staff have been made. Dr. Barrera Oro would need supplementary funds from the outside to get a respiratory

program going. Also, the salaries are badly in need of supplements to attract and maintain good people.

Connections. Dr. Barrera Oro has an excellent working relationship with the Pediatric Hospital (Pedro Elizaldo). Dr. Ricardo Carmona Gomez and Dr. Maria Isabel Berria are two young pediatricians who are extremely interested in participating in the clinical aspect of a program in respiratory disease. These persons appeared to be very serious, energetic and responsible. Both inpatient and outpatient studies are possible at the Hospital. Other clinical facilities in Buenos Aires could be made available to Dr. Barrera Oro if required.

3. General appraisal.

Dr. Barrera Oro is a knowledgeable and well trained virologist with a tremendous interest and enthusiasm for conduct of a good program in viral respiratory disease. He has already made a commendable start in spite of numerous handicaps and overwhelming obstacles. His facility, both laboratory and clinical, is excellent. He would do well to add a technical chief to the staff for the program and it would be desirable if some competent virologist from the outside could come in and work a year or two in rendering further training to the staff and in adding to the tissue culture facility. The real problem

at the Institute is one of unrest and failure of continuity in operation owing to problems in the area of administration. This seems a highly likely place for conduct of a respiratory research program provided the Institute can be stabilized and necessary additional funds become available.

B. University of Buenos Aires
School of Medicine
Buenos Aires, Argentina

Dr. Armando S. Parodi, Prof. of Microbiology and Parasitology (Dept. of Microbiology)
Dr. Norma E. Mettler, Chief, Arbovirus Laboratory.

1. Activities.

The Department of Microbiology carries a considerable teaching load in microbiology for medical students. The Department has been very active in studies of the Junin virus in Argentinian hemorrhagic fever. The virus apparently was first recovered by Dr. Parodi and his associates. Dr. Norma Mettler is now responsible for the arbovirus work. She recently returned to Argentina following an extensive training fellowship in Dr. Jordi Casals' laboratory at the Rockefeller Foundation Virus Laboratories in New York. Drs. Mettler and Parodi have published a number of papers on Junin virus and on Argentinian hemorrhagic fever. Dr. Mettler presently has a grant request to NIH/USPHS for funds to work on arboviruses. The level is for about US $23,000/yr.

Such respiratory virus research as is carried out is done by Dr. Parodi. Dr. Parodi has done considerable work with influenza and psittacosis in the past and has spent a great deal of time in the U.S.A. and Europe in connection with research activities. Dr. Parodi's interests are perhaps more inclined to basic rather than diagnostic research. Most recently, Drs. Lucia B. de Guerrero (biochemist) and Parodi published a report on changes in phosphoric acid metabolism in muscle of influenza-infected mice compared with muscle of control mice.

2. Resources.

Physical The physical plant available for respiratory virus research is somewhat modest. Some revision in the area to provide sterile rooms seems necessary. The tissue culture activity and facility also are limited. Animal space needs also to be added to.

Equipment. The laboratories are modestly equipped and funds for updating and expanding needed technical equipment would appear desirable.

Personnel. Dr. Parodi is conversant with and knowledgeable in the field of viral respiratory disease. He has heavy teaching responsibilities, however, and would need a strong person to head a program in respiratory disease such as he has in Dr. Mettler in the arbovirus activity. Dr. Parodi would like to

send Dr. Felis Garzon to the U.S.A. for a year of training in respiratory viruses provided that he can find the funds and the place. Technical people are available provided funds can be provided. The employees at the University are full-time. The inadequacy of staffing is amply illustrated in Dr. Mettler's paying the salary of one of her technicians from her own private resources.

Funds. Dr. Parodi would need funds for minor laboratory revision, for equipment and for support of technical persons including addition to his staff, clinical associates, and upgrading salaries to give permanence and competence.

Connections. Dr. Parodi has excellent connections with the Hospital of Niños (Gallo 1330, Buenos Aires). (Dr. Carlos Gianantonio is the chief of teaching and research.) This is claimed to be the largest children's hospital in the world. The physical evidence seemed convincing. There is a wealth of patient material, both in the hospital wards and in the clinics.

One most outstanding aspect is the presence there of Dr. Luis Becu who is chief of the department of pathology.

Dr. Becu is a highly trained Argentinian pathologist who took his basic training in pathology at the Mayo

Clinic in Rochester, Minn., where he spent 3 years. He spent 1 year in Sweden at the Caroline Institute studying cardiac disease in infants.

Dr. Becu is judged a very capable and energetic individual. He could command much higher salaries outside the Argentine but is dedicated to the need for helping in the development of his country's medical resources.

Dr. Becu might well be the focal point for a study of pathology in lethal viral respiratory disease in a cooperative study with Dr. Parodi.

3. General appraisal.

Dr. Parodi's interest and physical facilities are judged to be more consistent with some sort of basic research program or of studies of special cases of viral respiratory illness than, perhaps, in a large laboratory-epidemiologic investigation. This might be a location where some really fine work can be done on the viral etiology in infant deaths or in severe infantile pneumonia. There is an outstanding opportunity for a joint program between Dr. Parodi and Dr. Becu to ascertain viral etiology in severe respiratory illness and death in infancy. Gross and micropathologic descriptions of most viral infections are entirely missing in the literature. Here might be a unique opportunity for such important work.

Drs. Parodi and Becu exhibited great enthusiasm for conduct

of investigations in the respiratory field. The facilities and personnel, with outside support, could well be made completely functional and successful. There is a need for a competent virologist in the laboratory. Dr. Garzon, with a year's training abroad, might provide a good focal point for such virus work and it would be well to seek the assistance for a year or two of a trained virologist from the outside.

It should be added that respiratory disease is a most important clinical entity in Argentina. Epidemic bronchiolitis is extremely common. Respiratory disease ranks second in importance to diarrhea in pediatric illness in Argentina.

C. Institute of Virology
National Institute of Cordoba
Ayacucho 1643
Cordoba, Republic of Argentina

Director, José M. Vanella, M.D.
Subdirector, Juan C. Rivadeneira, M.D.

Drs. Vanella and Rivadeneira were not visited by Dr. Hilleman or by Dr. Lennette. On May 9, however, a completed questionnaire was submitted with a letter expressing interest in respiratory research in this facility. An explanatory report is therefore necessary.

1. Activities. Not defined. Apparently primarily a research institute.

Training. Training activity unknown.

Service. Service activity unknown.

2. Resources.

Physical. The Institute of Virology is located in a modern building and has a large laboratory facility for tissue culture, serology, and for animal breeding and animal utilization.

Equipment. Apparently inadequate. Would need equipment.

Personnel. In addition to Drs. Rivadeneira there are - Violeta Knez, Ph.D., Americo Marquez, M.D., Blanca A. Ramos, Ph.D., Lia S. Sack, M.D., who could be assigned to a program. Dr. Rivadeneira is presently a full-time worker in virology and would like to conduct a study in respiratory disease of viral etiology in Argentina.

Dr. Rivadeneira has had some experience in this field. During 1960 he started a study on the epidemiology of viral respiratory infections in children of Cordoba. Specimens for isolation and serology were collected from about 175 infants and children with respiratory disease and from 75 healthy controls. A total of 24 virus strains were isolated. No positive identifications were made although suggestive data were obtained. Serologic work also was done for influenza. The work had to be discontinued because of salary inadequacies.

Funds. Dr. Rivadeneira would need support from the outside to conduct the studies. Funds are not available from within. He would need money for professional assistance, for technicians and for the supporting clinical facility.

He would also need to send one or two persons elsewhere for advanced training and, ideally, should have some trained virologist to spend a year or so with him to help him set up the study.

Connections. There are no clinical facilities immediately available. All materials would have to be obtained from the University Hospital and from other private institutions.

3. General plan and appraisal. Dr. Rivadeneira, from the available data, appears competent and capable of carrying out a respiratory research program provided that he has adequate funds for equipment and for professional staff. He also will need to have funds for clinical assistance. Most important, is the aspect of training. Either someone will have to come from the outside to train the staff or Dr. Rivadeneira will have to send 1 or 2 persons abroad for specific training. Ideally, both should be done.

IV. Chile

A. (3/29-30/63) Institute of Bacteriology of Chile
Avenida Marathon 1000
Casilla 48
Santiago, Chile

Director of Dept. of Virology: Dr. Oscar Avendaño-Mondaca

1. Activities.

Service. The Institute of Microbiology is primarily a diagnostic and production laboratory. Dr. Avendaño produces rabies vaccine, smallpox vaccine, and is now making 30,000 doses of monovalent influenza A2 vaccine for use during the coming winter. He is employing the protamine process.

This is the only public health laboratory in Chile. Routine virus diagnoses are rendered for the various hospitals throughout the republic. Roughly 900 cases are studied per year. Dr. Avendaño routinely carries out tests for influenza, poliomyelitis, and Coxsackie and epidemic and murine typhus.

Dr. Avendaño has a good tissue culture production unit in operation. He prepares primary human amnion, F.L. line human amnion, HEpII, HeLa and primary monkey renal cell cultures. The monkey kidney cell suspensions are purchased from Microbiological Associates in the U.S.A.

Training. This is not a training center.

Research. The laboratory is not a research institute. Yet, Dr. Avendaño is a highly trained person, having spent ample time in the U.S.A., and is more than capable of conducting such investigations. In the conduct of his virus diagnostic activities, Dr. Avendaño has attempted recovery of a number of viruses from cases of respiratory illness, some of which have not as yet been identified. A beginning coordinated effort in this direction has been started in collaboration with the Children's Hospital.

2. Resources.

Physical. The Institute is housed in a building which is some years old but acceptable. There is adequate total space in the facility to handle a respiratory research program quite adequately. There are sufficient facilities for animals.

Equipment. The laboratory is moderately well equipped but could well be modernized and added to with considerable advantage.

Personnel. This is a real problem and supplementary funds for personnel will be required. Dr. Avendaño

has but a single highly trained technical assistant. This is Dr. Adriana McGinty. There are 4 allowed M.D.'s, 8 allowed laboratory technicians and 12 allowed laboratory assistants. The technicians are hand-trained high school graduates. The big problem is the pay scale. Pay is so low as to be unattractive to most trained people and, unlike most Latin American countries, the government specifically prohibits salary supplements using funds from the outside. It is permitted to add personnel using outside funds. In positions other than at the National Laboratory, personnel are allowed to take a second job to supplement income. This is prohibited at Dr. Avendaño's Institute.

Connections. Dr. Avendaño has good working connections with the hospitals so that proper specimens from respiratory disease cases could be obtained. The Children's Hospital (Hospital Roberto de Rio) under Dr. Arturo Scroggie would cooperate with Dr. Avendaño. Both in-patients and out-patients are available. Cooperation to return for follow-up blood specimens can be achieved readily by giving the parent 2 cans of milk. This device was used for the polio-vaccine studies.

The Microbiology Institute is part of the ministry

of health and, as such, is closely connected with Dr. Alfredo Leonardo Bravo (Chief, Technical Dept. of the Health Service) and Dr. Conrado Ristori. These people are available for consultation and for undertaking any special epidemiologic aspects of the investigation.

Dr. Ristori has brought together considerable information relating to respiratory disease in Chile. The population of Chile is 8,000,000. Twenty per cent of all deaths are of respiratory cause. This amounts to 18,000 deaths per year from respiratory disease. The majority of the cases are clinically bronchopneumonia. Respiratory disease is the principal cause of death in Chile.

Deaths are concentrated mainly in the very young and in the very old. During 1961, numbers of death ascribed to respiratory diseases were as follows:

1	yr.	9427	deaths
1- 4	"	2600	"
5- 9	"	370	"
10-14	"	162	"
15-19	"	139	"
20-24	"	153	"
25-34	"	312	"
35-44	"	366	"
45-54	"	530	"
55-64	"	818	"
65	"	3059	"

3. <u>General appraisal</u>.

Dr. Avendaño is a well trained and highly capable virologist who could very well undertake a study of viral respiratory

disease. His physical plant is adequate for the purpose although funds for equipment would be needed. Adequate clinical facilities can be made available to permit a good study. The principal problem at the Institute is the matter of salary and number of people. Outside funds would certainly effect an increase in the number of people available to do the work. The problem of permanence and quality would remain since supplementing of salaries is prohibited. This problem should not be considered as overwhelming, however. One additional matter relates to Dr. Avendaño's tenure. He will be able to retire in 2 years after 30 years' service and still at a relatively young age. If he chooses to retire, the program would be badly hampered, unless someone else were brought in and trained to take over.

B. School of Medicine
University of Chile
Santiago, Chile.

Dr. Guillermo Contreras, erudite enterovirologist, recently left the Bacteriological Institute to create a new Department of Virology in the School of Medicine.

Presently Dr. Contreras is heavily engaged in teaching and in building his department. Hence, he has no immediate possibility for a respiratory program. He does, however, have a very definite interest for such a program in the longer term.

V. Mexico

A. (3/25-26/63) Instituto Nacional de Virologia
Secretaria de Salubridad y Asistencia
Centro Medico del DF
Mexico, D.F., Mexico

Director: Dr. Carlos Campillo-Sainz

1. Activities

Research. Research on virologic problems began in this institute about 15 years ago. Currently and within recent years problems of poliomyelitis and of vaccination against poliomyelitis have been of primary interest. At the present time, interest and effort are focused on vaccination against poliomyelitis, vaccination against measles and also on studies on arboviruses.

The studies conducted are not concerned with basic or fundamental aspects but rather are directed at epidemiologic and clinical inquiries. Thus the work on arboviruses at the present time is a field epidemiologic study, chiefly a serologic survey of the Yucatán peninsula to determine what arboviruses are present in the population.

Some work on respiratory disease viruses is being conducted but this is confined entirely to influenza and the adenoviruses, and is primarily diagnostic in nature. There is a functioning tissue culture laboratory.

Training. This is not primarily a training center although occasional individuals have been accepted for varying intervals.

Service. This laboratory is not a service organization although a certain amount of diagnostic work, for example, in the respiratory disease field, results from its epidemiologic inquiries.

2. Resources.

Physical. This institute has the major portion of one floor in a wing of the Hospital for Oncology which is a fairly new building forming part of the complex comprising the Medical Center. The rooms are of a good size and at the moment one suite of two small laboratories is devoted to studies on influenza and adenoviruses. Several additional laboratories are occupied by personnel (entomologists and mammalogists) associated with Cornell University Medical College studies (Dr. William F. Scherer) in Mexico. Doctor Campillo is of the opinion that these two laboratories will become available within a year or so and can be assigned to an expanded program on respiratory disease. This space and perhaps more would certainly be required but Doctor Campillo did not feel that this would pose any problem. There appears to be ample animal space as well as adequate space for central service functions such as glassware washing and sterilization.

Equipment. The laboratory is fairly well equipped but will need additional equipment such as a Spinco preparative centrifuge, lyophile apparatus, tissue culture incubators, a refrigerator, a deep freeze, animal cages, etc. This is not to say that such items are lacking but rather that they will be needed in any expanded program dealing with the newer respiratory disease agents such as the coryzaviruses.

Personnel. The virologic experience of Dr. Carlos Campillo-Sainz goes back to 1946 when he spent one and one-half years under Doctors Eaton and Lennette at the Virus Laboratory of the California State Department of Public Health. He had additional training from 1952 to 1953 under Dr. John Enders at the Boston Children's Hospital.

To assist him in any respiratory disease studies that will be undertaken he has available a number of qualified and competent people. Dr. Alberto Nuñez Rivera is an epidemiologist with a wide experience in communicable diseases and is currently an instructor in epidemiology at the National School of Public Health in Mexico City. Dr. Lizardo Arreguin-Macin only recently had six months training at the respirovirus unit of the Communicable Disease Center at Atlanta, Georgia, and would participate to some extent in any respiratory disease program. He is

currently professor of microbiology at the Army Medical School in Mexico and an instructor in virology at the School of Medicine, National University of Mexico. Also available would be Dr. Eduardo Castro-Sierra who has had two years training in virology under Dr. Campillo and in addition to his appointment in the Institute is also an instructor in virology at the School of Medicine. Mr. Luis Enrique Sanchez-Torres at the present time is studying under Dr. Alick Isaacs at London and when he returns would be associated with respiratory disease studies. In addition there is Miss Enriqueta Pizarro-Suarez, who holds a Master's Degree from the University of Chicago and spent several months learning tissue culture techniques under Doctor Enders in Boston. Miss Pizarro, who is also professor of virology at the National Polytechnic Institute and professor of microbiology at the School of Medicine and the School of Dentistry, National University of Mexico, has been doing most of the respiratory disease work at the Institute and is assisted by a very capable associate, Miss Rafaela Zamudio-Banderas.

All in all, therefore, there is a highly competent group under Doctor Campillo and the nucleus of a more comprehensive respiratory disease study already exists. Doctor Campillo expressed the need for his staff to

acquire familiarity with techniques and procedures applicable to the study of the newer respiratory disease viruses and for serologic approaches, such as the new microtiter technique. He believes that this need would best be met not by sending personnel to the United States or elsewhere for training, but by having an experienced and well-trained virologist from Europe or the United States spend from six to twelve months, preferably more, in his laboratory assisting in organizing the new unit and training personnel in methodology. (It is of interest that other investigators in Central and South America expressed similar opinions, i.e., the virtual necessity of having a highly competent and experienced virologist from Europe or the United States assigned to the laboratory for teaching and training purposes.)

Funds. The laboratory derives its support from the Ministry of Health and a larger budget would be desirable to support more adequately the work that is presently going on. Any additional studies such as a small but comprehensive respiratory disease study would require funds of perhaps $15,000 to $20,000 beyond the present budget (Doctor Campillo's estimate). Ostensibly such funds would not be

forthcoming from the Ministry of Health and would have to be obtained from an outside source.

Connections. Inasmuch as the National Institute of Virology is a component of the Ministry of Health, it can call upon hospitals and public health centers anywhere within the Republic for assistance and also has available to it the resources of epidemiologic and vital statistics units.

3. General Plan and Appraisal.

Dr. Campillo is very much interested in organizing a study on viral respiratory disease and in view of his facilities and staff it would appear that he should be able to carry out such a program successfully. It would seem desirable to support concretely and adequately his desire to engage in this new area since no other unit in Mexico is in a position to undertake such studies in the near future. To implement his program Dr. Campillo will need funds, primarily to purchase equipment and a certain amount of consumable supplies, but also to obtain another one or two technicians. While competent professional help is available on his staff, two very important considerations arise. The first of these is the need to somehow supplement salaries so that the laboratory and field investigators will not be compelled to earn a living by holding several positions, thereby diffusing their efforts. Also highly

desirable is the bringing in of a consultant to participate actively in the work of the laboratory, thereby organizing its efforts and training its personnel.

B. (3/27/63) Instituto de Investigaciones Pecuarias (Palo Alto) Mexico D.F., Mexico

Virologist: Dr. Carlos España

1. Activities.

This laboratory, situated at Palo Alto on the road between Mexico City and Toluca, is devoted to diseases of domestic livestock. There is a central laboratory building and a number of barns and smaller buildings to house large animals. The laboratory building, which also houses a certain number of small laboratory animals, appears to possess a minimum of equipment although this is perhaps adequate for the type of work being pursued.

Dr. Carlos España, who studied under Dr. K.F. Meyer at the Hooper Foundation, University of California, San Francisco, and who earned his Ph.D. degree from the University of California in 1944(?), is currently working on anaplasmosis. Although trained as a virologist and still retaining his interest in this field in which he worked for a number of years, Doctor España's activities over the past few years have been on this problem, to which he has contributed materially. In his work he is assisted by his wife who earned her M.Sc. degree at the

University of California. Doctor España's work at the Institute is entirely investigative, apparently very little training being done. His laboratory is not at all concerned with service work. Much of his time, however, is pre-empted by teaching since he is on the staff of the National School of Biological Sciences of the National Polytechnic Institute. He does considerable teaching, not only formal lectures and some laboratory work in virology but recently has initiated a series of post-graduate seminars which are on a very high plane.

2. Resources.

As mentioned above, the laboratory appears to be adequately equipped for the work it is doing; additional equipment might be an asset in the studies currently being pursued although this was not discussed with Doctor España.

3. Possible Respiratory Disease Studies.

Doctor España's work on anaplasmosis has been conducted under the auspices and with the support of the University of Pennsylvania. Dr. Geoffrey Rake was the motivating spirit behind these studies and with his death an effective supporter of the work in Mexico was lost. There is thus the question as to whether the work which is done on a contractual basis will be continued at the expiration of the contract during the next year. However, it would appear that the University of Oklahoma may assume sponsorship of the studies at Palo Alto because of the importance of anaplasmosis in the southwestern United States and because of the interest of the University

of Oklahoma School of Veterinary Medicine in this disease.

As mentioned earlier Doctor España is, by training, a virologist and would like eventually to return to this field. If, therefore, the contract with the University of Oklahoma should not materialize, both he and Mrs. España would be available to undertake studies on viral respiratory disease, ostensibly under the auspices of the Institute.

Certain problems would, however, have to be met. First of all, it is uncertain how much support, monetary or otherwise, the Institute could contribute to non-veterinary problems. If space were available, funds presumably would be required to pay the salaries of additional technical and professional staff that would have to be recruited and considerable apparatus would have to be purchased, especially that concerned with tissue culture aspects of respiratory disease investigations. Thus, microscopes, roller drums, incubators, deep freeze boxes and refrigerators, magnetic stirrers, etc., etc. would have to be provided.

It would probably be most helpful to have Doctor España come to the United States for several months work in a respiratory disease laboratory. He is a very competent individual and could certainly do the necessary training of his technical staff. If however a competent virologist from the United States or Europe could be assigned to work with him during the initial organization phases of his laboratory, this would be most helpful.

Doctor España has very good connections with both teachers and clinicians and should he find it feasible to engage in viral respiratory disease studies, his past performance indicates that he would do a competent job and hence deserves serious consideration for support.

C. (3/26/63) Laboratorio de Virologia
Hospital Infantil de Mexico
Mexico D.F., Mexico

Director: Dr. Manuel Ramos-Alvarez

1. Activities.

Research. Dr. Ramos-Alvarez was trained under Dr. Albert B. Sabin and his primary interest has been and essentially remains enteroviruses. In his early studies in Mexico City, Doctor Ramos was concerned almost entirely with the central nervous system manifestations of enteroviral infections, but over the past several years he has been concerned solely with the problem of viral diarrheas and especially the possible role of enteroviruses in this syndrome. However his interests have encompassed the broad field of the diarrheas of infants and children and he has been attacking this problem with the active assistance and collaboration of a highly competent bacteriologist in the Children's Hospital. Much data of interest has emerged and Doctor Ramos-Alvarez is now in the process of preparing preliminary reports on his findings to date.

Training. This is not a training center.

Service. The laboratory provides no service functions such as diagnosis.

2. Resources.

Physical. Doctor Ramos-Alvarez's laboratory is very well equipped to carry out medical research of the type he has been engaged in. Since most of his work is based on tissue culture approaches, he has a well organized and efficiently functioning tissue culture laboratory. There are a number of sterile rooms for the preparation of cultures and for the inoculation of cultures. Animal rooms are also available but are small, in conformity with the small numbers of animals that are utilized.

Equipment. The laboratories are adequately equipped and could be converted to respiratory disease work without any difficulties. Additional animal space, however, might be required, especially for the preparation of type specific immune sera for the enteroviruses and the coryzavirus group.

Personnel. Doctor Ramos-Alvarez is a well-trained investigator with a considerable background of experience. Aside from the bacteriologist, he has no professional associates and does all of the virologic work himself with the assistance of a small group of capable technicians.

Funds. Doctor Ramos-Alvarez's work is supported by research grants from the National Institutes of Health. Were he at any time to convert his laboratory to respiratory disease problems, financial support ostensibly would come from the same sources.

Connections. Doctor Ramos-Alvarez works essentially on his own, utilizing clinical material obtained from the wards of the Children's Hospital. He is sufficiently well known and has sufficient prestige to obtain additional clinical material elsewhere or to secure collaborative participation of others but finds that for his viral diarrhea studies the Children's Hospital supplies all of the material he can use.

3. General Appraisal.

Dr. Ramos-Alvarez is a highly competent virologist who could unquestionably contribute materially to our knowledge of viral respiratory disease under the climatic and socio-economic conditions obtaining in Mexico. However he is quite content to pursue the studies which he is currently engaged in and indicated that he had no plans to change his present area of research interest for at least two years. He did state, however, that if he were to enter the field of viral respiratory diseases he would like to have a well-trained virologist from outside Mexico spend some months in his laboratory assisting him in training his personnel in the techniques and procedures necessary to pursue studies on these newer viral agents associated with respiratory disease. In essence, therefore, while Dr. Ramos-Alvarez is not interested at present in undertaking any studies on viral respiratory disease he is nevertheless interested in the general subject and it might be well to ascertain from time to time whether his interests are changing.

D. (3/27/63) Infectious Disease Research Laboratory
Hospital Infantil de Mexico
Mexico D.F., Mexico

Director: Dr. José Sosa-Martínez

This laboratory like that of Dr. Ramos-Alvarez is also housed in the Children's Hospital. Unlike the latter laboratory, however, that of Doctor Sosa is concerned with what in a sense might be considered a service function. In essence, Doctor Sosa provides diagnostic assistance through his studies on the etiology of central nervous system disturbances of presumed infectious origin. Doctor Sosa is a well trained and competent virologist who obtained his Ph.D. degree in virology at the University of California at Berkeley in 1953 or 1954; his thesis work, concerned with the epidemiology of herpes simplex virux infections, was done under Dr. Edwin H. Lennette. His unit at the Children's Hospital consists of two small laboratories, one in the basement and devoted to work, primarily serologic, on arthropod-borne viruses in Yucatan and another on the third floor devoted chiefly to his studies on the viral etiology of aseptic meningitis and other CNS disturbances.

The two units are rather small and additional floor space would be desirable even though Doctor Sosa to all intents and purposes works alone with two technicians. The two units contain a minimum of equipment such as centrifuges, incubators, etc., but the laboratory is relatively new and Doctor Sosa, using support obtained from the National Institutes of Health and from the Rockefeller Foundation is just beginning to get his work under way. His laboratory is included in this analysis because of his expressed interest in undertaking

work on viral respiratory diseases in the near future provided the necessary support is forthcoming. To implement any studies in this laboratory would necessitate first of all the securing of considerable more laboratory space than is presently available; additional animal space would probably be required, chiefly for the holding of animals being utilized for the preparation of immune sera of various kinds. Without doubt additional equipment would be necessary and the collaboration of a well trained and competent virologist would also be a requisite. Doctor Sosa, who is still a young man, has recently been acquiring recognition and stature in Mexico and it is felt that PAHO should maintain contact with him since such a liason can conceivably eventuate in a productive program on viral respiratory diseases.

VI. Costa Rica

A. (3/29/63) International Center for Medical Research and Training
Facultad de Medicina
Universidad de Costa Rica
San José, Costa Rica

Administrative Officer: Dr. Fred Payne
Laboratory of Virology: Dr. William Pelon

1. Activities.

Research. The Laboratory of Virology is part of the International Center for Medical Research and Training sponsored by and operating under the auspices of the School of Medicine, Louisiana State University, New Orleans, Louisiana and supported by special grants from the National Institutes of Health. The virus laboratory, like all of the other laboratory units

of this Center, is housed in the School of Medicine of the University of Costa Rica. The laboratory is essentially a new undertaking and the research under way at the present time is concerned entirely with the problem of infant diarrhea, especially its possible viral etiology. The clinical material being studied is obtained in large part from several study areas in which ICMRT is operating in Costa Rica. Additional clinical material for virologic examination is received from Doctor Leonardo Matta, virologist at the Instituto de Nutrición de Centro America y Panama in Guatemala City. Since all the stool material is examined in tissue culture systems, there is a very good tissue culture laboratory underpinning the virus laboratory.

Training. Training is a very important function of this laboratory and indeed this laboratory, as its name implies, was established for the purpose of conducting research into medical problems and for training people in the medical disciplines basic to such research. Students will be recruited from among those attending the Schools of Medicine, Dentistry, etc. in Costa Rica as well as elsewhere.

Service. The Center is not intended to operate as a service organization but to conduct research and training.

2. Resources.

Physical. The Center is housed in the Medical School which like all of the other buildings of the University is only a few years old. The virus laboratory consists of two large rooms subdivided into a laboratory proper and several cubicles

for sterile rooms. This provides space for the processing of tissues, the preparation of cell cultures, inoculation of cell cultures, the performance of serologic tests, etc. In conjunction with animal facilities available elsewhere in the building plus a small service area which holds incubators and/or refrigerators, lyophilization apparatus, etc., the present space is adequate although used to the maximum.

Equipment. The laboratories are very well equipped and if additional equipment is required, there would appear to be no difficulty to its acquisition.

Personnel. Doctor Pelon was trained in virology under Doctors William Y. Mogabgab and Sabin and is a competent investigator. His chief assistant appears to be Doctor Rhim, who received his training under Doctors Hammon and Melnick. Several technicians are available to assist Doctors Pelon and Rhim.

Funds. The support of the Center comes from National Institutes of Health grants to Louisiana State University School of Medicine (Dr. William H. Frye). If additional funds are required for the implementation of a program on respiratory diseases, this would presumably be in the form of a supplement to the present ICMRT grant.

Connections. The Center enjoys excellent working relationships with other departments in the Medical School and especially with the School of Microbiology whose director is Dr. Bernal Fernández, a very competent and highly respected microbiologist who has surrounded himself with an impressive

teaching and research staff. The existence of an epidemiologic unit within the framework of the ICMRT makes it feasible to obtain the necessary epidemiologic data, both in the nation as a whole as well as in those several areas where the Center is conducting certain studies.

3. General Plan and Appraisal.

Doctor Pelon indicates that his present studies on the possible viral etiology of diarrhea of infants and children should come to a conclusion within the next year to a year and a half, at which time he would very much like to undertake studies on viral respiratory disease. To effect such a change in the research program of the Center should occasion no difficulties since Doctor Pelon is a well trained virologist and in Doctor Rhim has a competent associate and laboratory supervisor. These two as a team could give the necessary guidance and direction to such a study without bringing in another professional person trained as a virologist although Doctor Pelon might eventually find that a second professional associate might be of considerable value in the project. There appears to be ample space in the Medical School (at least at the present time) to permit expansion of the virus laboratory should an additional one or two rooms be needed for extension of the work. Funding of the new inquiry should also pose no problem since the support can be obtained by augmenting the present grant by means of a supplement or by having Doctor Pelon apply directly to outside sources for a research grant. It is suggested that consideration be given to the possible establishment of a viral respiratory disease study in this laboratory.

VII. Panama

A. (3/30/63) Middle America Research Unit
Balboa Heights, Canal Zone, Panama

Director: Dr. Henry Beye
Virologist: Dr. Karl M. Johnson

1. Activities.

Research. The Middle America Research Unit represents a collaborative effort of the Walter Reed Army Institute of Research and the National Institute of Allergy and Infectious Diseases, National Institutes of Health. Both WRAIR and NIAID supply staff,the former supporting the mycological and bacteriological effort, the latter supporting the virologic and field (epidemiologists, mammalogists, entomologists, etc.) effort. More specifically, the Middle America Research Unit represents the field arm of the Laboratory of Tropical Virology of the National Institute of Allergy and Infectious Diseases, the Laboratory of Tropical Virology supplying the officer in charge of MARU. Although some bacteriological and mycological work, for example in histoplasmosis, is being done the major effort is concerned with the arthropod-borne viruses. At the time of this report virtually all of the virologic and field resources of the laboratory were being diverted to a fire fighting operation, namely an inquiry into the etiology and transmission of Bolivian hemorrhagic fever, which has been encountered in a wide area of Bolivia in the Amazon basin and which has resulted in the virtual abandonment of

a number of towns over the region. Previous studies have been concerned with outbreaks of Venezuelan equine encephalomyelitis in both man and equines in Panama and on the epidemiology of St. Louis encephalitis virus infections in Panama.

Because of the importance of respiratory disease from both the morbidity and mortality standpoints in Panama, Dr. Karl M. Johnson was assigned to the unit to study the viral respiratory disease problem. However his efforts at the present time are being directed towards resolution of the problem of hemorrhagic fever in Bolivia.

Training. The Middle America Research Unit is not basically a training center in microbiology or virology although indirectly it does provide training through the assignment of young physicians who have entered the Public Health Service in lieu of military service. Also, provision is made to accept established investigators who would like to spend some time studying virologic problems under ecologic conditions obtaining in Panama.

Service. MARU was not intended to be a service organization except in the sense that such service is incident to the epidemiologic study of outbreaks of infectious disease in various parts of Middle America.

2. Resources.

Physical. Over the last three years much has been done to increase the laboratory facilities of MARU. The laboratories and offices on the first floor of the building have

been revamped and an entirely new set of laboratories has been provided on the second floor together with an expansion of the animal facilities. Excellent laboratories of ample floor space are available for the preparation of tissue cultures, for serologic and virus work, for bacteriology, for mycology, for centrifugation, for incubation, for refrigeration, etc. Ample space exists for expansion of laboratories in the future.

Equipment. The laboratory is very well equipped for medical research in both the laboratory and the field. Since it is not the purpose of the laboratory to pursue research on very basic or fundamental aspects of virology, equipment such as an electron microscope, analytical centrifuge, etc. is not available and not required.

Personnel. Dr. Karl M. Johnson is the only virologist in the unit although Dr. Arnold Monto, a young physician serving a two-year tour of duty in the Public Health Service, has been assigned to him for training. In addition, Dr. R.B.Mackenzie a physician trained in epidemiology at the School of Public Health, University of California at Berkeley is available for consultation and actual participation in the arbovirus and other studies.

Funds. The unit is supported primarily with funds from the National Institute of Allergy and Infectious Diseases as an intramural operation. The current level of support does not appear to be adequate to take care of operations conducted

on a scale as are those currently in Bolivia, i.e., neither sufficient travel money nor personnel are available to have this unit function at the level at which it should be operating. To support studies on viral respiratory disease would require increasing the operating budget to take care of both consumable supplies and travel as well as providing personnel.

Connections. MARU enjoys an excellent working relationship with many countries of Middle America and locally can utilize the various Health Centers in the Canal Zone as well as the clinical facilities of the Gorgas Hospital, the Santo Tomas Hospital and also the Children's Hospital (Hospital del Niño). The establishment of MARU has served to stimulate the Gorgas Memorial Laboratory into a reassessment of its programs and accomplishments and led it to undertake new projects. Whatever the outcome, in terms of success and productivity, of the new program of the Gorgas Memorial Laboratory might prove to be, a certain amount of rivalry will unquestionably develop. As a consequence, it seems reasonable that there will be little if any duplication of effort and that a respiratory disease program, if one is to be set up in Panama, would more logically be set up under the auspices of the Laboratory of Tropical Virology in the MARU component.

3. General Plan and Appraisal.

Although Dr. Karl M. Johnson was assigned to the MARU laboratory in July 1962 to organize a laboratory for the study of viral

respiratory disease, other problems have precluded his doing so. The most important has been the problem of the Bolivian hemorrhagic fever to which, as mentioned above, virtually all of the virologic and field resources of the laboratory have been allocated. Doctor Johnson himself is shortly to leave for San Joaquin, Bolivia, where Dr. Henry Beye and the Bolivian Ministry of Health have established field stations and a laboratory at Magdalena. Doctor Johnson's assignment is of indefinite duration but rather effectively interferes with his desire to undertake work on viral respiratory disease.

To establish such a laboratory, Doctor Johnson has at the present time Dr. R. B. Mackenzie, who would participate as the epidemiologist, and Dr. Arnold Monto, who is being trained as a virologist and would assist Doctor Johnson in the laboratory phases as well as in the clinical aspects. It seems reasonable, however, that if the program is to be set on a secure footing Doctor Johnson will need the collaboration or assistance of a full-time virologist on a permanent basis as well as the assistance of an epidemiologist in the field. Laboratory space and equipment apparently present no problem but additional funds will be required in order to add technicians to the laboratory staff. How much supplemental financial support is required at the present time is unknown, but it appears certain that no additional personnel can now be obtained because of the limited funds allocated by NIAID to the Laboratory of Tropical Virology. Doctor Johnson is an old hand in the viral respiratory disease field. His laboratory, if established, could undertake no only serologic surveys of

resident populations but also a hospital surveillance of respiratory disease and also a longitudinal study of the resident population. Ideally his unit should also have the facilities for the preparation of diagnostic reagents, both antigens and type specific immune sera. Finally but not least, his unit could assist materially in the field in which more assistance is needed, namely that of evaluation of vaccines devised against the many respiratory disease viruses that are being isolated today. The establishment of a respiratory disease laboratory at MARU will undoubtedly require discussions between PAHO and the NIAID and it is suggested that exploratory discussions be initiated with Dr. Alexis Shelokov, Director of the Laboratory of Tropical Virology, NIAID and with Dr. Dorland Davis, Associate Director, Intramural Programs, NIAID.

VIII. Venezuela

A. (4/3/63) Instituto Nacional de Higiene
Caracas, Venezuela

Director: Dr. Antonio L. Briceño-Rossi
Enterovirus Laboratory: Dr. Henri Fossart

1. Activities.

Research. The National Institute of Hygiene is both a research and a service organization. It has research activities covering bacteriology, mycology, parasitology, immunology and virology.

With specific reference to viral problems, the Institute has worked on a number of diseases including the epidemiology of Venezuelan equine encephalomyelitis,

influenza and adenoviruses. The work on respiratory viruses is limited to influenza and adenoviruses and is under the direct supervision of Doctor Briceño-Rossi. He is also in charge of the work being done on arthropod-borne viruses and has working under him Dr. Luque Hernández who is being trained, according to Doctor Briceño-Rossi, to take over the responsibilities of work on the respiratory viruses. Dr. Henri Fossart is in charge of the enterovirus laboratory and apparently has the only tissue culture operation in the Institute.

Training. The Institute does some training although this is not one of its leading objectives.

Service. The Institute is a service organization in the sense that it produces a number of biologics, has a Food and Drug Control Laboratory, etc. One of its aims is to establish a viral diagnostic laboratory but this is still in the very early stages and the organizational pattern has yet to be established, as will be noted below.

2. Resources.

Physical. The Institute is housed in a building which is about twenty years old, and shows the effects of excellent maintenance and good custodial care; in brief the building is beautifully maintained and could serve as a model of cleanliness for many laboratories, including those in the United States. The

space appears to be well utilized but any program on viral respiratory disease would have to be allocated space at the expense of other activities since the laboratories currently engaged in virologic research would prove inadequate from the standpoint of floor space.

Equipment. The laboratories are quite well equipped although the virologic laboratories themselves would need considerable additional equipment to permit them to do the necessary tissue culture and serologic work.

Personnel. As mentioned above, the current respiratory disease laboratory is under the direction of Doctor Briceño-Rossi who is training Dr. Luque Hernández to assume eventual responsibility for this unit. Doctor Fossart, as indicated earlier, is in charge of the enterovirus laboratory and if an adequate level of study is to be undertaken of the respiratory disease problem, not only more technicians would be needed but probably professional personnel as well. This is because of the manifold activities of the present staff, all of which leads to a thin coverage. Thus Doctor Fossart, although he is in his laboratory at the Institute from 8 A.M. until 3 P.M., also has the responsibility for teaching microbiology at the Medical School and this takes much of his time. He has no assistants in his teaching and must handle it all himself, eight lectures per week plus laboratory

sessions.

Funds. Additional support from outside would be required to support any studies on viral respiratory disease since the present budget permits of no expansion and it is doubtful if additional funds can be obtained from government sources in the near future.

Connections. Since the Institute is located on the grounds of the Medical School complex, ample clinical facilities are available. In addition there exists a division of epidemiology, headed by Dr. Alejandro Principe, which provides epidemiologic assistance and also collects vital statistics, all of this information being published annually in a rather large volume two or three inches thick.

3. General Plan and Appraisal.

Both Doctor Briceño-Rossi and Doctor Fossart expressed considerable enthusiasm for undertaking studies in viral respiratory disease. However there appear to be differences in approach and in philosophy that will have to be reconciled before a respiratory disease unit can be established. Thus considerable thought will have to be given by the director, Doctor Briceño-Rossi, as to exactly how a respiratory disease laboratory would function under Dr. Luque Hernández, when many of the newer viruses (coryzaviruses) fall into the enterovirus group or very closely resemble them in their properties and behavior. In brief, the establishment of such a unit would lead to an overlap with the enterovirus laboratory headed by Doctor Fossart. A priori, it might seem

desirable to incorporate such a respiratory disease unit into Doctor Fossart's present operation; he is a very competent virologist especially in the enterovirus field (trained under Dr. Henry Gelfand at the Communicable Disease Center, Atlanta, Georgia and under Dr. Hanna Doany, PAHO Consultant, then at the Tissue Culture Laboratory in Cali, Colombia) and could quickly acquire the additional skills by a two- or three-month soujourn in a respiratory disease laboratory in the United States. Union of these two activities, however, might lead to other unforeseen difficulties and hence consideration might be given to the operational pattern followed in the Viral and Rickettsial Disease Laboratory of the California State Department of Public Health. One of the functions of this laboratory is routine diagnosis but the laboratory has rather effectively and successfully wedded its routine and research activities to provide a smoothly functioning diagnostic operation. Whatever approach is used, the Institute appears to offer a promising environment for respiratory disease studies and exploration of this possibility is to be encouraged.

Additional Comment

Although already mentioned, it should be re-emphasized that in the visits made by both Dr. Lennette and Dr. Hilleman virtual unanimity of opinion was expressed that re-training of people and re-organization of virus laboratories are best accomplished by having a competent virologist from abroad spend a year or more in the particular laboratory rather than sending staff from these laboratories for individual training abroad.

Also, it will be desirable for PAHO to seek means for getting a maximum of the interested Latin American investigators in this field to the VII International Congresses of Tropical Medicine and Malaria in Rio de Janeiro, to participate in the working groups that are meeting at the same time under PAHO sponsorship.