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VIRUS RESEARCH FACILITIES
IN CENTRAL AND SOUTH AMERICA

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The epidemiology of virus infections of humans and animals requires studies in many fields other than virology alone. This discussion is concerned with the facilities and resources available for epidemiologic studies.

There are many classifications and groupings of viruses, most of which have some degree of artificiality about them. I am going to outline here an artificial grouping that will be useful for this discussion. I shall consider the viruses involved in induction of disease in humans and domestic animals in two groups, nonarbovirus and arbovirus.

Viruses in the nonarbovirus category include the poliomyelitis agents, smallpox, the influenza viruses, measles, mumps, rubella, chickenpox, adenoviruses, reoviruses, coronaviruses, and herpesviruses. A unifying epidemiologic concept for all of them is that they are viruses that can maintain themselves in nature solely in human populations. Vectors are not required. Nonhuman vertebrates, although occasionally involved with certain of these viruses, are not essential for their existence. Various recent findings with the monkeypox virus in Africa and with influenza A virus might require some modification of the above statement. As a corollary of the above definition, these viruses are found wherever people are found anywhere in the world. They are extensively studied in laboratories in many countries.

In addition to these nonarboviral agents that cause human disease, there are a number implicated in animal disease, including foot-and-mouth disease virus, myxomatosis (transmitted mechanically by insects), and many other agents.

Particular interest has attached to certain viruses in the above listing--notably the poliomyelitis agents, smallpox, measles, rubella,

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and influenza--since vaccines against them were developed. A gap still remains with respect to the effective use of the vaccines now available, however, and for many of the Latin American and Caribbean countries the problem is acute. Limited health department budgets for purchase or manufacture of a vaccine, for administration where needed, and for epidemiologic follow-up after vaccination may cripple the best-intentioned efforts.

It is becoming evident that an efficient monitoring system is required to check on the effectiveness and coverage of a vaccine and to follow the immune status of a population in periods between vaccination. Such a system must be continuously sieving the population, using already known virologic techniques, to determine antibody rates and levels. The object of such a program is to identify those subsets of the population, possibly defined by age group, sex, geographic location, or socioeconomic stratum, or by associations of such variables, that have been inadequately immunized through vaccination or natural virus activity. Then immunization can be selectively carried out. Such a procedure obviously leads to the most rational and effective use of a vaccine.

Such studies are not easy. Even if the laboratory end has been reasonably well standardized, problems and questions beset the interpretation of field study results. Research has shown that following oral administration of trivalent polio vaccine, conversion rates in the tropics are lower than in temperate zones. Several studies are being directed toward a more complete understanding of this phenomenon. A more rational immunization protocol should result from these studies.

It is becoming increasingly evident that for the nonarboviral infections of man, each country, or in some instances an epidemiologically defined group of several of the smaller countries, requires a well-endowed and -staffed virus laboratory capable of monitoring the human population continuously and on quite a large scale. It will not be possible to rely in the future on the cooperation extended by friendly outside laboratories. Laboratories that can provide such monitoring service exist in Argentina, Brazil, Chile, Colombia, Cuba, Ecuador, Jamaica, Mexico, Panama, Peru, Trinidad, Uruguay, and Venezuela, but in

few instances are they equipped and staffed to operate at a level that will provide effective predictive monitoring. All too often the laboratories are one- or two-man shows, operating on a shoe string and with a radius of effective activity encompassing only a limited geographic zone within a country. Services to outlying districts, away from the local capital, decrease at some power greater than the square of the distance.

The recent poliomyelitis outbreak in Trinidad, which resulted in 180 cases and 19 deaths, was predicted by the Trinidad Regional Virus Laboratory on the basis of low antibody rates in children plus an accelerated rate of polio-2 virus recovery preceding the outbreak. The outbreak was caused by polio-1. The same laboratory is now signalling the existence of low rubella antibody rates in the same population. Prediction of a rubella outbreak is a logical sequitur.

The existence of arboviruses adds another dimension. This assemblage of viruses shares certain common features. They require an arthropod for transmission from one vertebrate host to another (in the basic cycle of the virus), and, excepting the dengue viruses and possibly some of the phlebotomus viruses, each has a reservoir in some or several subhuman vertebrates. Epidemiologically, these requirements restrict the movements of each virus. Although arboviruses are distributed worldwide, any given agent has a more limited range, defined by the existence of a suitable vector(s) and a suitable host(s). A list of important North and South American arboviruses, known to cause illness in man, includes yellow fever, dengues, and eastern, western, California, and Venezuelan encephalitis, as well as a few less frequently encountered agents such as Oropouche, Mayaro, and Ilheus. This is not a complete listing. The total list of arboviruses in the region is much longer--some 160 at latest count. Most of these have not yet been linked to any significant amount of human or livestock disease. To this list is often appended the Tacaribe group, including Junin virus, the causative agent of Argentinian hemorrhagic fever, and Machupo, the causative agent of Bolivian hemorrhagic fever. No arthropod vectors of these viral relatives of lymphocytic chorio-meningitis have been incriminated, but most of them appear to require a subhuman (rodent) reservoir.

The conditions for a given arbovirus limiting certain arthropod vector(s) and vertebrate host(s) mean that the arboviruses encountered in one country will probably not be identical with those in another. Similarities are more likely to be found in ecologically similar regions of several countries. This leads to the concept of regional laboratories for the investigation of arboviruses. Investigations required are not entirely of virologic nature by any means, although a sound virologic basis is essential. Such investigations require participation of entomologists, ornithologists, mammalogists, and broadly oriented ecologists in multidisciplinary teams. Such laboratories and teams are difficult to staff and expensive to operate. Operating costs go up sharply when there must be an active program in the field as well as at the bench.

Those few laboratories of this nature that have existed or do exist in the Caribbean and Latin America have repeatedly demonstrated their utility by showing the activity of yellow fever in several countries; by recognizing on several occasions the occurrence and following the sweep of dengue through the circum-Caribbean zone, and by recognizing the outbreak and following the spread of Venezuelan equine encephalitis and making recommendations for its control. Laboratory groups equipped and staffed to carry out the intricate multidisciplinary studies required for large-scale arbovirus work are listed in Appendix I.

Not all of the laboratories operate on a large scale, and the larger laboratories, with well-staffed teams and ambitious programs, number less than half a dozen.

Laboratories engaging in epidemiologically oriented virus investigations have a few special administrative and financial problems. Vector insects and host vertebrates do not observe international boundaries. Similarly, epidemics of the nonarboviruses may move freely and rapidly through human populations. Therefore, there must be provision for international extension of activities on short notice. Laboratories with sole support from a single government are usually hampered by inability to get into action quickly when an epidemic occurs. Government budgetary and personnel controls are often so restrictive that it may take days or weeks to get a team into the field. Therefore, there must be provision for

fluid funds. In this connection, flexible funding by an outside agency can be far more valuable than the actual cash commitment. Appendix II shows a representative budget.

An assessment of current laboratory facilities able to cope with arbovirus epidemiologic studies is a discouraging exercise. The withdrawal of Rockefeller Foundation staff and support from the laboratories in Trinidad, Belém, and Cali has been a crippling blow to each. They have continued to function on a reduced basis. The threatened withdrawal of U.S. Government support from the Middle America Research Unit in the Canal Zone is a grave matter. The University of São Paulo arbovirus program may also be seriously threatened.

The programs are so expensive that to operate them on a regional basis appears justified and indicated. Any laboratory with a multi-disciplinary program will require at least \$150,000 per year, including all salaries, and could easily use \$450,000 or more if it were to operate a comprehensive program. This wide range of budget figures should not be taken to indicate loose calculation. Instead, it represents the spread between a skeletal program and an adequate though not exaggerated one.

Possibilities for financing include national sources, international agencies, and foundations or interested philanthropies. It is not realistic to anticipate any appreciable funds from industry. Universities are sometimes eager to use existing laboratory facilities for graduate or post-graduate training, but are loath to provide compensatory funding. National funds to provide an assured maintenance level, and extra-national funds to permit program extensions in various directions are the desirable solution.

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Postscript:

To locate every health department, medical school, research institute, or other facility in Latin America where some type of virus work has been, is being carried on, or is projected is beyond the scope of this discussion.

A series of qualifications must be made, not to define what has been done, but rather the limits of what I, personally, know something about.

First, the plant and insect viruses are left for someone else to cover. Excellent work in both these areas has been and is being done in various Latin American centers.

This leaves us with the animal viruses or--more properly--viruses affecting vertebrates. Here, again, I exclude from discussion a very important virus belonging to this group, namely foot-and-mouth disease virus. There are both national and international laboratories in several countries dedicated almost exclusively to studies of this virus.

Rabies, a very important virus affecting both animals and man, receives scant attention here, beyond remarking that facilities for routine diagnosis of rabies exist in most countries. In some countries, rabies vaccine is also produced. A few centers have epidemiologically oriented programs that emphasize investigations of rabies problems in humans and domestic animals. Such programs include studies on the dog, mongoose, and bat reservoirs of rabies virus.

Further to limit the field, those laboratories engaged primarily or entirely in basic virologic studies are also excluded. Such studies, involving expensive equipment and centered upon a virus per se, rather than being concerned with the interaction of a virus and a human or animal vertebrate population, can be carried on anywhere in the world where adequate equipment and trained workers exist. There are no geographic limitations.

APPENDIX I

Laboratories with Interest in Epidemiologic Plus
Virologic Investigations of Virus Diseases in Man

Mexico	Instituto Nacional de Virología, Instituto de Salubridad y Enfermedades Tropicales
Colombia	Instituto Nacional de Salud, Bogotá Universidad del Valle, Cali Universidad de Antioquia, Medellín
Trinidad	Trinidad Regional Virus Laboratory
Jamaica	University of the West Indies
Panama	Gorgas Memorial Laboratory/Middle America Research Unit
Venezuela	Instituto Nacional de Higiene Instituto Venezolano de Investigaciones Científicas
French Guiana	Institut Pasteur, Cayenne
Brazil	Instituto Evandro Chagas, Belém Instituto de Microbiologia, Rio de Janeiro Instituto Adolfo Lutz, Laboratorio de Arbovirus
Peru	Instituto de Salud Pública, Lima
Argentina	Instituto Malbrán, Buenos Aires Universidad de Buenos Aires Universidad de Córdoba

APPENDIX II

TRINIDAD REGIONAL VIRUS LABORATORY EXPENDITURE AND AVERAGE NUMBER OF STAFF
1952-68

Year	Funds - US\$			Total	Average staff during year		
	Rockefeller Foundation	United Kingdom	Caribbean Governments		Professionals	Technicians	Other
1952	44,500	-	-	44,500	2	3	19
1953	56,303	-	-	56,303	2	5**	29
1954	80,056	-	-	80,056	4	11	37
1955	70,838	6,672	6,672	84,182	4	11	40
1956	52,557	22,720	22,720	97,997	4	13	40
1957	59,296	25,374	25,374	110,044	4	11	39
1958	70,632	27,139	27,139	124,910	4	11	39
1959	65,961	31,971	31,971	129,903	4	12	40
1960	67,163	34,055	44,944	146,162	4	11	48
1961	66,695	30,703	46,055	143,453	7	13	36
1961	189,221*	-	-	189,221*	6	13	40
1962	62,223	36,966	55,449	154,638	5	13	41
1962	412*	-	-	412*	5	15	41
1963	79,531	59,507	48,688	187,726	6	16	44
1964	83,933	59,803	48,929	192,665	5	18	43
1965	109,197	59,215	48,448	216,860	4	14	36
1966	73,772	61,914	50,657	186,343	5	14	43
1967	93,324	72,661	59,449	225,434	5	14	43
1968	49,213	53,048	43,402	145,663	4	14	36
TOTALS	1,374,827	581,748	559,897	2,516,472			

* Building funds

** 1954 through 1968, includes British Medical Research Council Senior Laboratory Technician