Pan American Health Organization

PAHO/ACMR/21/3
Original: English

TWENTY-FIRST MEETING OF THE
PAHO ADVISORY COMMITTEE ON MEDICAL RESEARCH

Caracas, Venezuela
29-30 April 1982

WHO COLLABORATING CENTERS IN THE REGION OF THE AMERICAS. THEIR ACTIVITIES.

WHO COLLABORATING CENTERS IN THE REGION OF THE AMERICAS. THEIR ACTIVITIES.

Presented by G. A. Schmunis

SUMMARY

The WHO Collaborating Centers are national institutions that cooperate with ongoing WHO programs at national, regional and global levels. Although their primary role as national institutions is to contribute through research, training and providing services to national health development, they also participate in globally conceived and directed WHO schemes of collaborative activities conducted under WHO's initiative.

There are 162 WHO Collaborating Centers in the Region covering a wide range of program areas from human reproduction, communicable diseases or classification of diseases to laboratory technology, traditional medicine or veterinary public health. More than half of them are located in the USA. Although designation of an institution as a WHO Collaborating Center does not indicate commitment by the Organization concerning financial support, centers attached to some WHO program received significant financial aid. Others receive very limited sums and most of them do not get any monetary support. However, the WHO label often enables the institution to obtain further financial support from other sources. Thus the catalytic role of the Organization is fully accomplished.

It is expected that the different networks of Collaborating Centers on the Region will be expanded and a more even geographical distribution reached. A better distribution of centers by program areas should be also obtained. There is a need for centers devoted to health services research and appropriate technology in the different disciplines, as well as centers engaged in research, training and service in support of the programs on diarrheal diseases and nutrition. The fact that the Collaborating Centers are increasingly being used in relation with institutional support to technical cooperation programs at country level may well improve the overall balance.

I. BACKGROUND

The idea of using national institutions for international activities goes back to the days of the League of Nations, when national laboratories were designated as reference centers for standardization of biological products. Beginning in 1947, WHO appointed more reference centers, starting with the World Infuenza Center, in London, for worldwide epidemiological surveillance. Since 1958, and together with the expansion of the WHO program for medical research, the number of such centers has been increased.[1] This evolution is a logical one as national institutions dealing with health research and training have a key responsibility in the development of national health research programs, and constitute an indispensable basis for WHO's collaborative research activities, on the national, regional and global levels. Some of these reference institutions are named as WHO Collaborating Centers and include their domain of responsibility in their title.[1,2]

The primary role of the WHO Collaborating Centers, as national institutions, is to contribute through research and training to national health development. Furthermore, they participate in globally conceived and directed WHO schemes of collaborative research conducted in regional or interregional frameworks under WHO's initiative.[1,2]

Until now the network of WHO Collaborating Centers has played and is continuing to play an important role in the development of WHO's program, in particular its research component.[1] Probably, the most positive feature of this mechanism is that all these centers have been created and are functioning in already existing institutions.[1] This concept is in agreement with the WHO established policy, that the Organization should not have its own international research institutions but should assist, coordinate and make use of the activities of existing institutions in order to best advance the field of research in health.[3,4]

A broader perspective of the nature and functions of the centers is being considered. The Collaborating Centers are viewed not only as institutions that collaborate with ongoing WHO programs, but also as a part of a strategy for strengthening country resources for national health development.[1,2] Thus, the centers should have a strong role in trying to solve the problems of their respective countries. It should not be overlooked that the Collaborating Centers are primarily national institutions. Mainly in developing countries one of their chief functions is to cooperate in the development of national health services, and to stimulate improvement of other local institutions. This promotional aspect is of vital importance as a means of encouraging the creation of a national infrastructure to support epidemiologic or other research activities and the provision of increased and better services.

The Organization policy of technical cooperation lays strong emphasis on strengthening institutions in developing countries and the international recognition, which is provided to institutions designated as Collaborating Centers, is considered by itself as mechanisms of institutional strengthening.

a) Criteria for selection of institutions

In general, the following criteria are taken into consideration in designating an institution as a WHO Collaborating Center.[1,5]

1. The scientific and technical capability of the institution as assessed at the national and international levels, with particular reference to its most recent work.

2. The place held by the institution within the country's health science and educational structure, its relations with the pertinent national authorities with respect to its contribution to the execution of health programs, and the governmental support it receives.

3. The quality of its scientific and technical management, the number and qualifications of its technical staff, and the adequacy of its equipment, laboratories and teaching facilities, as well as other resources.

4. The future stability of the institution, in terms of personnel, activity, and operation.

5. The working relations established between the institution and other institutions in the country or at international and regional levels.

6. The ability and willingness to contribute to the activities of WHO programs and the support of national programs or to participate in international collaborative programs.

7. The institution's desire to develop its potential appropriately with WHO scientific and technical support.

8. The ability and willingness of the institution to provide services over a sufficient length of time and not only for a short-term specific task.

b) Functions

The functions performed by the WHO Collaborating Centers, severally or collectively, include the following[5]:

1. Collection, synthesis and dissemination of information. For example concentration of technical and scientific information required for their activities, and dissemination of the information generated by these activities; b) distribution of information of interest to health agencies of the countries and/or required for better implementation of WHO programs; c) exchange of information among centers, particularly among those constituting a regional or world-wide network.

2. Standardization of terminology and nomenclature of technology, of diagnostic, therapeutic, and prophylactic substances, and of methods and procedures. For example international classification of diseases; b) establishment of international standards and reference preparations for biological substances used in human or veterinary medicine; c) international histopathological nomenclature and classification of tumors, etc.

3. Development and application of appropriate technology.

4. Provision of reference substances and the other services. For example: production and provision of reference chemicals and materials. Services are geared in general to the requirements of programs of world-wide interest. As an example, during 1975-1976, the viral disease program, through the pertinent centers, supplied national laboratories in more than 40 countries with 4,000 strains of virus, 30,000 ml of antigens, 9,000 ml of corresponding sera, 4,000 ml of receptor-destroying enzyme, and more than 50 different tissue cultures.

5. Participation in collaborative research developed under the Organization's leadership, including the planning, conduct, monitoring, and evaluation of research, as well as promotion of the application of the results of research.

6. Research training.

7. Coordination of activities on a given subject carried out by several institutions. The centers should coordinate the national activities in their area of competence and also coordinate their own operation with that of the regional and global networks in such a way that there is joint, well-oriented and well-informed participation in efforts for the study and eventual solution of problems affecting one or more countries.

II. PAST AND ACTUAL DEVELOPMENT OF THE SYSTEM

The growing interest of WHO in seeking the support of national institutions as Collaborating Centers is well expressed by the fact that in 10 years (1969-1978) the number of centers for different program activities has risen from 168 in 34 countries to 582 in 62 countries,[1] (Figure 1).

In 1978, 50.5 per cent of the WHO Collaborating Centers were in Europe, and 26.6 per cent in the Americas, the rest in the Western Pacific (7.4 per cent), South East Asia (4.7 per cent), Eastern Mediterranean (6 per cent), and Africa (4.8 per cent)[1] Regions (Figure 2). A break-down of the areas of activities of those centers at global level is shown in Table 1. The evolution of the number of centers since 1948 in the different program areas, within the Region of the Americas, is shown in Figure 3.[1]

Judging by the number of Collaborating Centers designated up to 1978, it would appear that the Americas is a Region that has made rapid progress in collaboration and support of WHO programs at this time. However, a break-down of the number of centers in the developing (USA and Canada) and the underdeveloping countries of the Region (all the others) showed that in 1980, 61 per cent of the centers were located in the USA and Canada (Figure 4).

The uneven distribution of centers in different WHO Regions (Figure 2, Table 1), and in some countries above others within a Region (Figure 4), may be explained by the fact that WHO Collaborating Centers are dealing mainly with biomedical research or provide reference and information services of highly technical character. Since they provide for the organization the best expertise available, they have been selected from among the institutions with the highest scientific and technical standing and with the best international reputation. These institutions, mainly from developed countries, must retain their place in the system. However, institutions from developing countries, which show a growing capacity to fulfill a function or functions related with the Organization's program at the country, subregional, regional, and global level may also qualify for designation when they may play a role in national and/or international health development and are contributing to increase technical cooperation with and among countries.

Figure 1

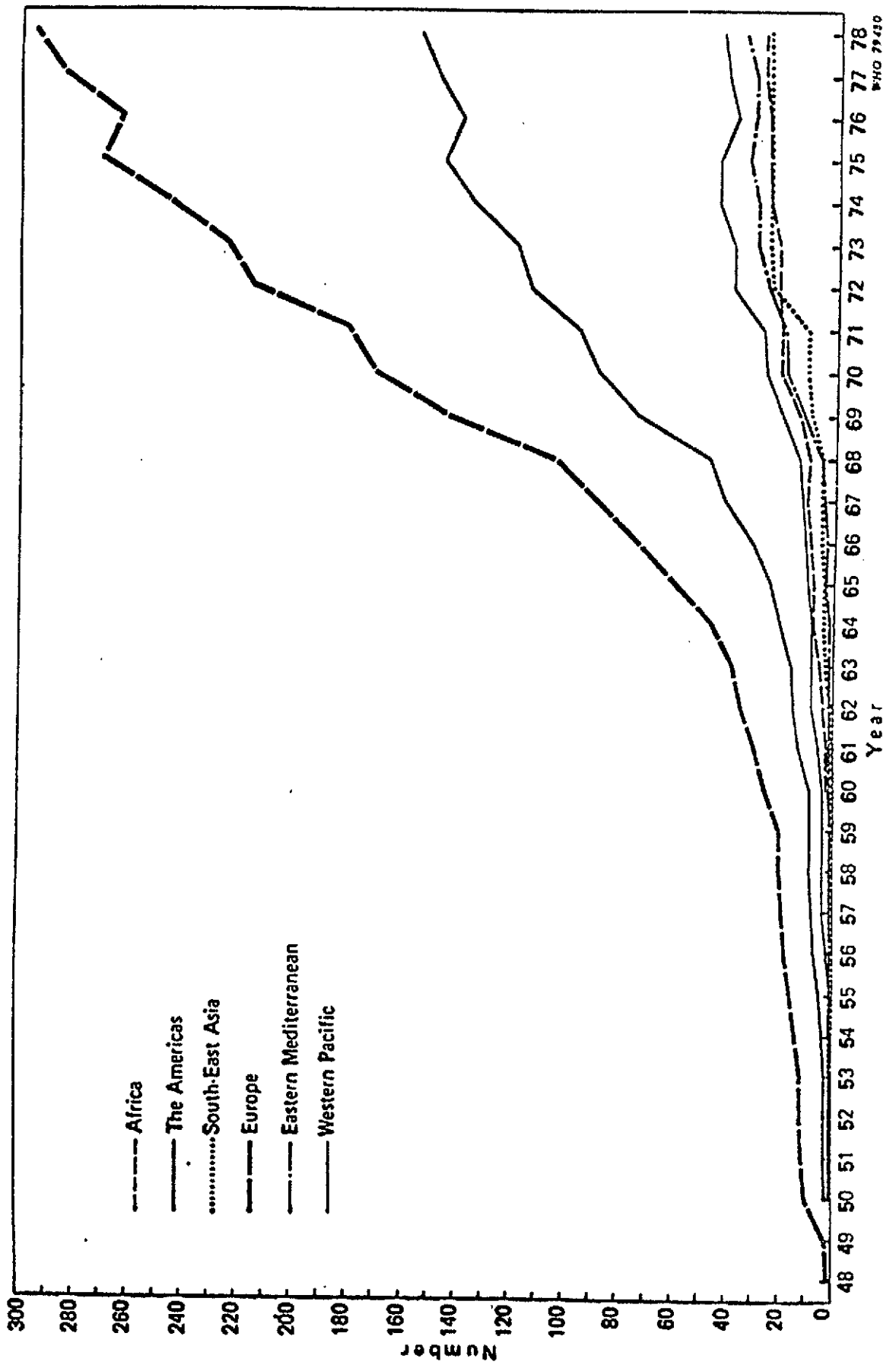

NUMBER OF WHO COLLABORATING CENTRES IN OPERATION, BY REGION AND BY YEAR (1948–1978)
Africa
The Americas
South-East Asia
Europe
Eastern Mediterranean
Western Pacific
Number
Year
0
20
40
60
80
100
120
140
160
180
200
220
240
260
280
300
48 49 50 51 52 53 54 55 56 57 58 59 60 61 62 63 64 65 66 67 68 69 70 71 72 73 74 75 76 77 78
WHO 79430

Figure 2

DISTRIBUTION OF WHO COLLABORATING CENTERS IN OPERATION IN 1978, BY REGION

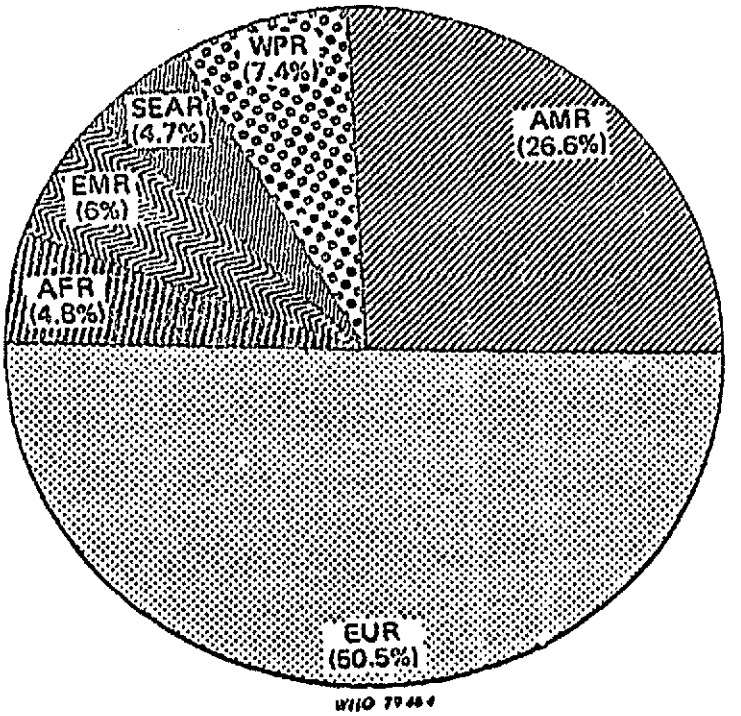


Table 1

MAJOR PROGRAM OF ACTIVITIES OF WHO COLLABORATING CENTERS IN THE DIFFERENT WHO REGIONS IN 1978

MAJOR PROGRAM	AFRO	AMRO	SEARO	EURO	EMRO	WPRO	TOTAL
Development of Integrated Hlth. Servs.	7	35	13	66	9	11	141
Development of Health Personnel	-	2	-	3	3	-	8
Disease Prevention & Control	12	82	7	164	12	23	300
Promotion of Environmental Health	9	33	7	57	10	9	125
Health Information	-	3	-	4	1	-	8
TOTAL	28	155	27	294	35	43	582

AFRO: Africa Region; AMRO: Region of the Americas; SEARO: South-East Asia Region; EURO: European Region; EMRO: Eastern Mediterranean Region; WPRO: Western Pacific Region.

Figure 3

NUMBER OF WHO COLLABORATIVE CENTERS IN OPERATION
BY SECTOR AND BY YEAR

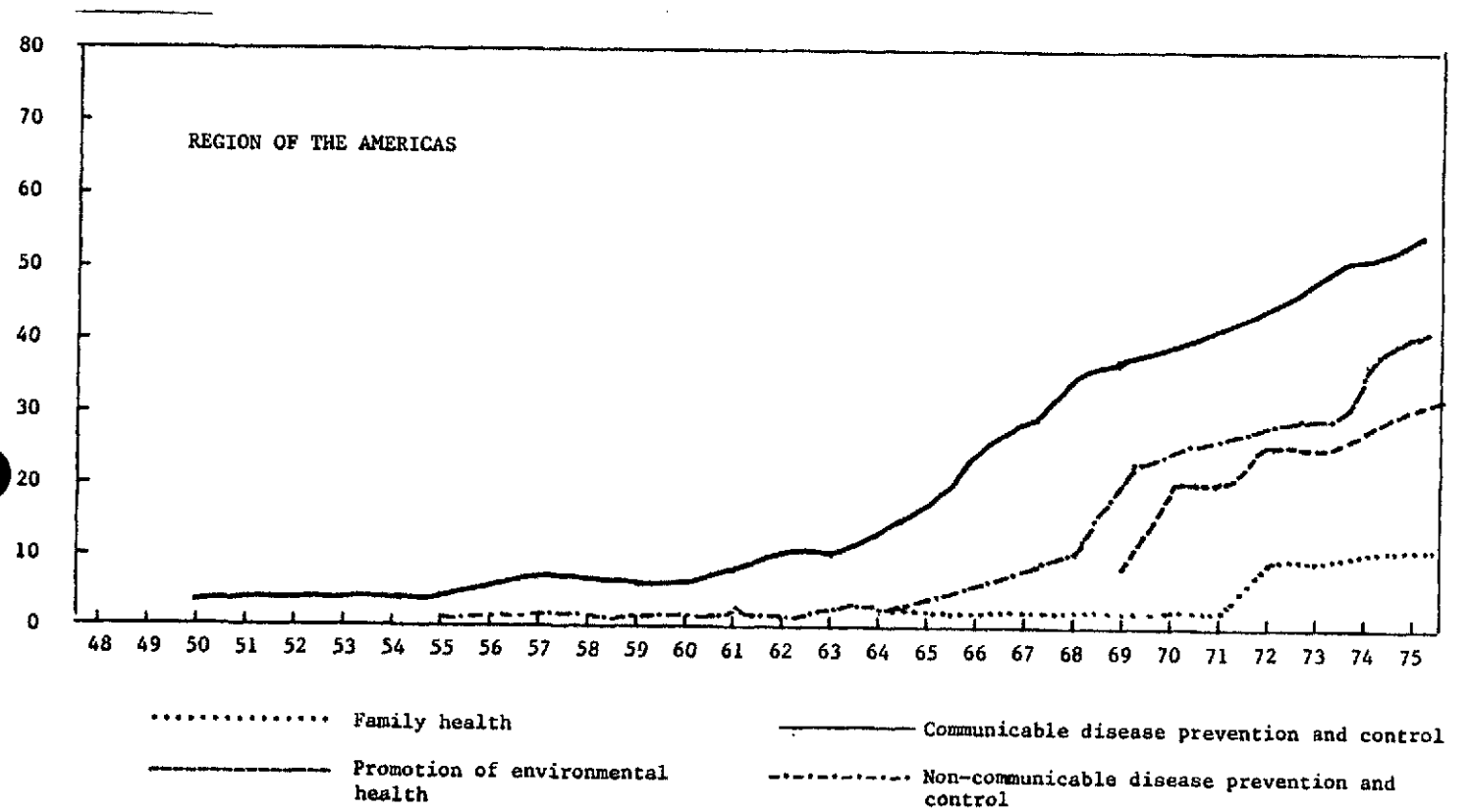
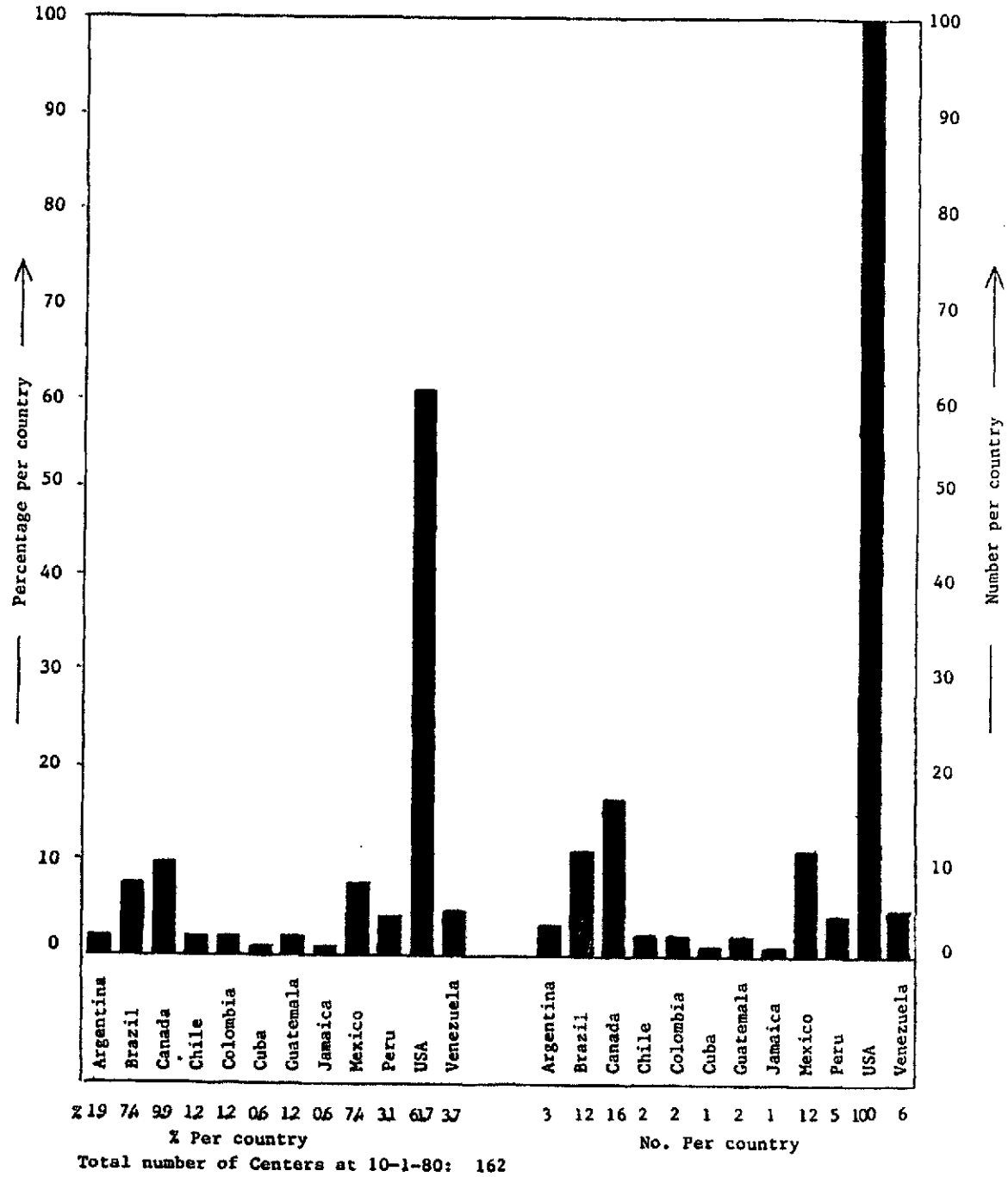


Figure 4

PERCENTAGE AND TOTAL NUMBER OF COLLABORATIVE CENTERS
PER COUNTRY IN THE AMERICAS IN 1980



III. COLLABORATING CENTERS IN THE AMERICAN REGION

The designation of a center is only the starting point of a dynamic process of collaboration involving active working contacts. Those centers which do not fulfill their proposed tasks or are no longer needed are dropped from the system (in fact six centers were terminated during 1981); those which performed well are redesignated (30 during 1981). Furthermore, new institutions are continuously being identified and selected for designation following the needs of the different programs (six during 1981).

a) Financial support

Although designation of an institution as a WHO Collaborating Center does not indicate any commitment by the Organization concerning financial support, until 1980 a substantial amount of money ($10.685.428) was chaneled by the Organization to the Centers (Table 2).

The total amounts shown in Table 2 should be taken with caution. Some of the programs allocate considerable financial aid to the Centers, e.g., human reproduction; while others only provide very limited sums, e.g., viral diseases. Moreover, quite a number of Centers do not receive any monetary support even though they contribute significantly to the work of the Organization. However, nomination as Collaborating Center often enables the institution to obtain further financial support from its own government, other international agencies, or from private sources. Thus, the catalytic role of the Organization is fully accomplished.

b) Activities

Until recently, the relationship between the Centers and the Organization was mostly with Headquarter's offices in Geneva. Although usually mutually appreciated, and with some of the Centers more fructiferous than with others, the relationship with regional offices was weak or non existent.[1,2] This situation is changing now as the Region participates more actively in all WHO program activities.

At the end of 1981 there were in the Region 162 Collaborating Centers located in 13 countries. Their activities were related to the following program areas: a) health services development; b) family health; c) mental health; d) prophylactic, diagnostic and therapeutic substances; e) communicable diseases; f) non-communicable diseases prevention and control; g) promotion of environmental health; h) health manpower development; i) health information; j) traditional medicine and k) oral health (Table 3).

Table 2

FINANCIAL AID PROVIDED BY WHO TO COLLABORATING CENTERS IN THE DIFFERENT COUNTRIES OF THE REGION UNTIL 1980*

Countries	Amount		
	Until 1979	1980	Total
Argentina	2.228.505	320.540	2.549.045
Brazil	1.231.200	294.700	1.525.900
Canada	372.653	42.272	414.925
Chile	-	150.760	150.760
Colombia	-	98.950	98.950
Costa Rica	-	5.000	5.000
Cuba	566.500	116.000	682.500
Mexico	1.039.001	126.574	1.165.575
Peru	26.000	6.000	32.000
USA	3.530.123	349.490	3.879.613
Venezuela	177.160	4.000	181.160
Grand total	9.171.142	1.514.286	10.685.428

*Centers active at December 1981.

Some of the support is related with their activities as WHO Collaborating Centers, but was not given to them because they are Collaborating Centers. To one Center in Argentina, part of the funds received were provided by other programs of the Organization and were not related with its activities as a Collaborating Center.

Table 3

PROGRAM AREAS AND COUNTRIES OF WHO COLLABORATING CENTERS IN THE AMERICAS

Programme Area \ Country	Argentina	Brasil	Canada	Chile	Colombia	Costa Rica	Cuba	Guatemala	Jamaica	Mexico	Peru	USA	Venezuela	Total per Program. in the Americas
Health Services Development[1]	1	1	1	1						2		7		13
Family Health[2]	1	2	1	1	1		1			3		1		11
Mental Health			3		2					3		5	1	14
Prophylactic Diagn. and Therapeutic Substances[3]			1									3		4
Communic. Diseases Prevention & Control[4]	1	4	2			1		1	1		1	47	1	59
Non-communic. Diseases Prevention & Control[5]	1	2	2							1		14		20
Promotion of Environ. Health[6]	1	5	4					1		1	4	15	1	32
Health Manpower Develop.										1		1		2
Health Information[7]		1										1	1	3
Traditional Medicine										1		2		3
Oral Health												1		1
Total per Country	5	15	14	2	3	1	1	2	1	12	5	97	4	162

* December 1981

[1] Workers health, Care of the Aged, Health Laboratory Technology, Radiation. [2] Maternal and child health, Human reproduction. [3] Biologicals. [4] Bacterial Diseases, Diarrhoeal Disease Control, Leprosy, Venereal Diseases and Treponemotosis, Viral Diseases, Veterinary Public Health. Smallpox erradication, Prevention of Blindness, Vector Biology and Control, Parasitic Diseases. [5] Cancer, Cardiovascular Diseases, Human Genetics, other Non-communicable Diseases, Immunology. [6] Basic sanitary measures, Recognition and control of environmental hazards, Food Safety. [7] International Classification of Diseases.

Because of the nature of this report and the number of Centers in the Region, it is impossible to make a detailed account of the activities of all Centers. Annex 1 shows a listing of all Collaborating Centers in the Americas, active at December 1981, including their terms of reference. However, as an example, some highlights concerning the activities of some of the networks of Collaborating Centers is reported below.

Collaborating Centers in Human Reproduction

At national level, the Centers give advice to the family planning program and conduct research on local problems. Their activities are aimed toward achieving self-reliance in research while at the same time mobilizing the capabilities of many countries for both, research training and consultant expertise. There is a continuous promotion of active collaboration among scientists of different countries thereby increasing the international pool of knowledge and technology. The Centers also conduct multicenter studies. They are part of a world-wide network that can assess the safety of current methods of fertility regulation and test new methods on rural and urban areas.[6]

The different areas of research in which the Centers were involved are shown in Table 4. A Center's participation in a study depends on a number of factors: national relevance of the method; conformity with national drug regulatory requirements; geographic distribution of Centers for the trial to determine possible population differences; workload of the Center in terms of other ongoing trials; director's interest; feasibility in terms of availability of adequate numbers of subjects for the study; and availability of staff and appropriate facilities. Although selection of institutions, organization, and management of the studies has been difficult because of the multinational nature of the projects, the results in general have been extremely good. A valuable by product of this kind of research was the establishment of local ethics committees in a number of institutions since ethical clearance of all protocols is required.[6]

Collaborating Centers on Viral Diseases

The development of a network of Collaborating Centers for reference and research on viruses began in 1947 with the setting up of a World Influenza Center in London by the Interim Commission of WHO to carry out the world-wide surveillance of influenza. A second Center was soon created for the Americas (CDC, Atlanta, Georgia, USA). At present, institutions from national influenza centers are linked with the two Collaborating Centers through WHO.[1,7] The Center in Atlanta has agreed: a) to obtain, fully characterize and preserve representative strains from outbreaks in different parts of the world and distribute them to research and vaccine production laboratories; b) to advise on the strains which should be included in influenza vaccines; c) to arrange for the training of research workers in specialized techniques; d) in collaboration with the Virus and Epidemiological Surveillance Units at WHO

Table 4

MULTICENTER STUDIES IN THE COLLABORATING CENTERS FOR CLINICAL RESEARCH[1] AND RESEARCH AND TRAINING[2] IN HUMAN REPRODUCTION IN THE AMERICAS (1980)*

Countries / Research Areas	Cali[1] Colombia	Canada[1]	Havana[1] Cuba	Mexico City[1] Mexico	San Salvador El Salvador[1]-	Santiago[2] Chile
Oral contraceptives		X	X	X	X	X
Intrauterine devices	X	X	X	X	X	X
Injectables			X	X	X	X
Determination of fertile period						X
Female sterilization	X	X	X	X		
Abortion			X			
Prostaglandins			X			
Vaginal rings	X		X	X		
Infertility	X	X	X	X	X	

*Adapted from ref. 6

in Geneva, to collect and distribute epidemiological information about the prevalence of influenza in different parts of the world; and e) to provide reagent kits for the national influenza centers.

In two relatively recent outbreaks caused by viruses A/New Jersey/76 and A/USSR/77, the reagents, antigens, and antisera were distributed to the national influenza centers within less than three weeks. High yielding recombinant viruses for vaccine preparation were put at the disposal of vaccine producers within four weeks. The same operations required three months in 1968.[7]

The problems raised by large epidemics of poliomyelitis and the development of a killed vaccine, together with the confusion existing in the description of new strains of Coxsackieviruses and Echoviruses, led to a series of collaborative studies under WHO aegis and the creation of a network of WHO reference centers in 1953. In 1958 this scheme was extended to all other viruses of public health importance. In 1973 the distinction between centers dealing with enteroviruses and respiratory viruses was abolished since many of the centers were in fact working in both fields.[7] At present there are in the Region 17 Collaborating Centers in four countries (14 in USA, and 1 in Brazil, Canada and Jamaica respectively) (Table 5). For practical reasons a distinction has been maintained for influenza, viral hepatitis, mycoplasma, arboviruses, special pathogens, rickettsiae, and those centers which have a specific task rather than a wide range of reference activities. Recent advances in certain fields such as hepatitis and special pathogens has led to the addition of new centers to cover these subjects.[7]

The terms of reference of the viral diseases Collaborating Centers are: to provide reference services (identification of rare strains); to prepare and distribute to national laboratories reference sera, antigens, and strains; to take part in collaborative studies; to cooperate with national laboratories and provide them with advice and training; to give on request advice to governments and assistance in epidemics; to collect epidemiological information; and to carry out applied research. This represents a considerable return to the WHO technical cooperation program in exchange for the limited grants which are given to the centers.[7]

Some of the specific activities are worth mentioning. One is the direct technical cooperation of Collaborating Centers with countries. As an example, during an outbreak of Rift Valley fever in Egypt in 1977, the Collaborating Center for Arbovirus Reference and Research (Yale University, New Haven, USA) identified the responsible virus in less than two weeks. Furthermore, personnel of the Center together with the regional WHO office staff, personnel of the local reference center and local authorities, drew up a program for the prevention of further outbreaks. A second trend aims at the strengthening of national virus laboratories particularly in developing countries. The success of the

network of national influenza centres is being used as a model on which to build a network for surveillance of other diseases of international public health interest. A network of national centers for the surveillance of viral hepatitis is under consideration, with the WHO Collaborating Center in Phoenix, Arizona, USA, responsible for the production and distribution of kits and reagents for the ELISA Technique for the diagnosis of this disease.[7]

In view of the importance given by WHO at this moment to the development of a Control Program of Acute Respiratory Infections in Children in developing countries and the prominent role that viruses have as etiological agents of these infections, it is envisaged that some of the Collaborating Centers participating in the network of viral diseases will actively cooperate with the ARI program. In fact, the Center in Maryland (National Institute of Allergy and Infectious Diseases) is already studying the possibility of using cold-adapted strains as a possible vaccine candidate to prevent Respiratory Syncitial virus, the major etiologic agent of bronchiolitis and pneumonia in early life.

Activities of other Collaborating Centers

Concerning other aspects of respiratory infections, a Collaborating Center in Philadelphia, USA (School of Medicine, University of Pennsylvania) is already collecting strains of pneumococci and information on prevalent serotypes and provides typing sera and reference strains and reagents to national laboratories. It is evident, that in view of the multiplicity of serotypes of pneumococci, and the differences in their geographical distribution, a real need exists for surveys and typing in order to prepare vaccines with the proper antigenic composition.

Almost all Centers in the Region, besides providing services and doing research, offer training and research training. If one considers that for strengthening the research and service capabilities in developing countries a critical mass of personnel has to be created to form the core of institutional support, these training activities are one of the most important functions of the Collaborating Centers. As an example, the Centers on Immunology, Pediatric Pathology and Mycosis (Sao Paulo and Rio de Janeiro, Brazil and San José, Costa Rica respectively offered courses sponsored and partially financed by the Organization in which dozens of nationals and students from other neighboring countries of the Region acquired training in those subjects. It is clearly desirable to have institutions offering training in the same language and in host countries with similar health problems of those of the trainees.

Table 5

WHO COLLABORATING CENTERS IN VIRAL DISEASES IN THE AMERICAS

Area of Activity	Institution	Location
Reference and research on influenza	Centers for Disease Control	Atlanta, USA
For virus reference and research	Centers for Disease Control	Atlanta, USA
	Centers for Disease Control	Atlanta, USA
	National Institute of Allergy and Infectious Diseases	Bethesda, USA
	Baylor College of Medicine	Houston, USA
For reference and research on viral hepatitis	Centers for Disease Control	Phoenix, USA
For mycoplasma reference and research	National Institute of Allergy and Infectious Diseases	Bethesda, USA
For arbovirus reference and research	Centers for Disease Control	Fort Collins, USA
	Yale University	New Haven, USA
For virus reference and research (special pathogens)	Centers for Disease Control	Atlanta, USA
Virus Collaborating Centers	Institute Adolfo Lutz	Sao Paulo, Brazil
	Laboratory Center for Disease Control	Ottawa, Canada
	University of West Indies	Kingston, Jamaica
For cell cultures	American Type Culture Collection	Rockville, USA
For rickettsial reference and research	University of Maryland	Baltimore, USA
	National Institute of Allergy and Infectious Diseases	Hamilton, USA
	Centers for Disease Control	Atlanta, USA

It is interesting that, despite the renewed and growing interest of the scientific community in the Region in tropical diseases and the importance of the Organization program in this area, there has been slow growth in the number of Centers devoted to the subject. However, in the last two years four centers were designated whose activities, in one way or another, are devoted to study different aspects of these diseases. The one located in Buenos Aires (Institute Fatala Chaben) has just finished a serologic survey on Chagas disease on 217,500 military recruits. The results showed a decrease in the transmission of American trypanosomiasis (from 10.1 to 6.0 per cent) in those born after the beginning of the national campaign for the control of this disease. The Center in Rio de Janeiro (Instituto Oswaldo Cruz) is performing studies on humoral and cell mediated immune responses in man and animals infected with Trypanosoma cruzi and Leishmania. This is the only institution in South America that is maintaining in captivity a breeding colony of Rhesus monkeys and making them available for studies on experimental T. cruzi infection. It also produces and provides monoclonal antibodies against T. cruzi, as well as local strains of T. cruzi and leischmania to researchers interested in the subject. The Center in Colombia (Malaria Eradication Service) is engaged in the evaluation of new pesticides, pesticide formulations, and pesticide application equipment for the control of triatomid bugs and anopheles mosquitos. The Center in Atlanta, (Centers for Disease Control) performs field studies on the epidemiology and control of malaria; develops methodology for antimalarial quantification and in vitro sensitivity testing, as well as guidelines for the production of serological reagents and also provides Plasmodium falciparum reference material and human standard sera for serology.

IV. FUTURE DEVELOPMENTS IN THE REGION

It is expected that the different networks of Collaborating Centers on the Region will be expanded and a more even geographical distribution reached.

Better distribution of Centers by program areas should be also obtained. There is a need for centers devoted to health services research and appropriate technology in the different disciplines, as well as centers engaged in research, training and service in support of the program on diarrheal diseases and nutrition. The fact that the Collaborating Centers may be used in relation with institutional support to technical cooperation programs at country level may well improve the overall balance.

REFERENCES

1. WHO, Doc. EB65/1980/REC/1(OP/2), Annex 6.

2. A plan for the management of research in WHO. WHO Doc. DEO/78.2.

3. WHO. Res. WHA 2.19, 1949.

4. WHO. Res. WHA 2.32, 1949.

5. WHO Manual, X7 pp. 7-12, 1978.

6. WHO Special Programme of Research, Development and Training in Human Reproduction. 9th Annual Report, 1980.

7. WHO Doc. EPC/EBWG/5, 1978.