ı Report of the Director
National Heart, Lung, and Blood Institute

Volume 5.
Companion Issues

U.S. Department of Health
and Human Services
Public Health Service
National Institutes of Health

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Tenth Report of the Director
National Heart, Lung, and Blood Institute
Ten-Year Review and Five-Year Plan

Volume 5.
Companion Issues

U.S. Department of Health and Human Services
Public Health Service
National Institutes of Health
NIH Publication No. 84-2360

Preface

The National Heart, Lung, and Blood Institute is now in its fourth decade, following its original establishment in 1948 as the National Heart Institute (P.L. 80-655). With a growing awareness of national health problems over the years, such as those reflected in the President's Conference on Heart Disease and Cancer (April 21, 1961) and the President's Commission on Heart Disease, Cancer, and Stroke (December 9, 1964), it was redesignated by the Secretary of Health, Education, and Welfare (now Health and Human Services) as the National Heart and Lung Institute (NHLI) in 1969. The activities of the Institute were expanded in 1972 by the National Heart, Blood Vessel, Lung, and Blood Act (P.L. 92-423) to advance the national attack on diseases of the heart, blood vessels, lungs, and blood. With the passage of the Health Research and Health Services Amendments in 1976 (P.L. 94-278), in which the NHLI was redesignated as the National Heart, Lung, and Blood Institute, the authority was further enlarged to include research on the use of blood and blood products and on the management of blood resources.

The 1972 act was of special significance. The law mandated that the Director of the Institute, with the advice of its Advisory Council, develop a national plan for attacking heart, blood vessel, lung, and blood diseases. The need for the plan evolved from a recognition that isolated approaches were no longer appropriate to the growing magnitude of these public health problems. Twenty-eight task groups of approximately 250 medical and scientific advisors assessed these problems and identified new opportunities for initiatives. The effort culminated in the five-volume National Heart, Blood Vessel, Lung, and Blood Program (DHEW Publ. Nos. (NIH) 73-515, 73-516, 73-517, 73-518, 73-519, 73-520, 73-521, 73-522, and 73-524). The needs, goals, recommendations, and strategies presented in the document provided a National Program, which for the past decade has been updated annually and has guided the Institute. The process includes:

- Research on the epidemiology, etiology, and prevention of heart, blood vessel, lung, and blood diseases
- Research on basic cardiovascular biological processes
- Development and evaluation of techniques, drugs, and devices to aid diagnosis and treatment

- Programs to develop technological devices to assist, replace, or monitor vital organs
- Field studies and large-scale tests relating to those diseases
- Research on blood diseases and the use of blood resources in the United States, including such items as collection, preservation, fractionation, and distribution
- Education and training of scientists and clinicians
- Public and professional education programs in all aspects of those diseases
- Programs to research and study heart, lung, blood vessel, and blood diseases of children.

The 1972 act also requires the Director of the Institute to submit an annual report to the President, for transmittal to Congress, on the accomplishments of the National Program during the preceding year and on plans for the next 5 years.

This five-volume Tenth Report of the Director, NHLBI, commemorates the 10th anniversary of the National Program. Volume 1 is an overview and summary of the other four volumes. Volumes 2, 3, and 4 report on program areas (table 1) of the Division of Heart and Vascular Diseases, Division of Lung Diseases, and Division of Blood Diseases and Resources. This final volume is on companion issues, and it discusses matters with an Institute-wide rather than divisional basis:

- Program coordination and liaison
- Prevention, education, and control
- International programs
- Research training and development
- Legislative history.

The process by which these volumes were developed was modeled after the one used in 1972 for the National Program. Members of working and review groups were drawn from the NHLBI staff, the Advisory Council and advisory committees, the extramural scientific community, the community of health providers and health consumers, and the general public.

Table 1. Program Areas of the National Heart, Lung, and Blood Institute

Division of Heart and Vascular Diseases	Division of Lung Diseases	Division of Blood Diseases and Resources
Arteriosclerosis	Structure and function of the lung	Bleeding and clotting disorders
Hypertension	Chronic obstructive pulmonary disease	Disorders of the red blood cell
Cerebrovascular disease	Pediatric pulmonary diseases	Sickle cell disease
Coronary heart disease	Fibrotic and immunologic interstitial lung diseases	Blood resources
Peripheral vascular disease	Respiratory failure	
Arrhythmias	Pulmonary vascular diseases	
Heart failure and shock		
Congenital and rheumatic heart disease		
Cardiomyopathies and infections of the heart		
Circulatory assistance		

Contents

Figures

Tables

1. Program Coordination and Liaison

Contents

1. Program Coordination and Liaison

The Interagency Technical Committee

A requirement of the National Heart, Blood Vessel, Lung, and Blood Act of 1972 (P.L. 92-423) was that the Secretary of Health, Education, and Welfare establish an Interagency Technical Committee (IATC) on Heart, Blood Vessel, Lung, and Blood Diseases and Blood Resources to coordinate "those aspects of all federal health programs and activities relating to heart, blood vessel, lung, and blood diseases and to blood resources to assure the adequacy and technical soundness of such programs and activities and to provide for the full communication and exchange of information necessary to maintain adequate coordination of such programs and activities" (Section 416). The legislation further required that the Director of the National Heart and Lung Institute (after 1976, National Heart, Lung, and Blood Institute) serve as chairman of the IATC and that all Federal departments and agencies with programs involving functions or responsibilities in the areas of heart, blood vessel, lung, and blood diseases and blood resources be represented. The original IATC membership and the membership in 1982 are shown in table 2.

The IATC meets twice a year. The meetings give the member agencies the opportunity to exchange information on the status of their programs. Such discussions facilitate the coordination of research activities and help eliminate duplication and overlap of efforts.

For fiscal years 1972, 1973, and 1974, the IATC published annual reports on Federal support and interagency cooperation in research related to the National Program mandated by Public Law 92-423. Rounded total expenditures are displayed in table 3.

In 1977, the IATC reported again on research activities in the National Program areas*. The first volume of the report, "Progress Through Coordination," provided an overview of the IATC's coordination efforts and described other interinstitute, interagency, and international collaborative efforts not directly

*DHEW Publication Nos. (NIH) 78-1475 and 78-1476.

Table 2. IATC Member Agencies

Original Members 1972	Current Members 1982
Department of Health, Education, and Welfare (DHEW):	Department of Health and Human Services (HHS):
Food and Drug Administration (FDA)	Alcohol, Drug Abuse, and Mental Health Administration (ADAMHA)***
Health Services and Mental Health Administration (HSMHA)*	Centers for Disease Control (CDC)***
National Institutes of Health (NIH)	Food and Drug Administration (FDA)
Social and Rehabilitation Services (SRS)	Health Resources and Services Administration (HRSA)
Social Security Administration (SSA)	Office of Health Research, Statistics and Technology (OHRST)
Other Agencies:	Other Agencies:
Atomic Energy Commission (AEC)**	Department of Defense (DOD)
Department of Agriculture (USDA)	Department of Energy (DOE)
Department of Defense (DOD)	Department of Transportation (DOT)
Department of Transportation (DOT)	Environmental Protection Agency (EPA)
Environmental Protection Agency (EPA)	National Aeronautics and Space Administration (NASA)
National Aeronautics and Space Administration (NASA)	National Institutes of Handicapped Research (NIHR)
National Science Foundation (NSF)	National Science Foundation (NSF)
Veterans Administration (VA)	Rehabilitation Services Administration (RSA)
	U.S. Department of Agriculture (USDA)
	Veterans Administration (VA)

*Renamed the Health Services Administration in 1973.
**Transferred to the Energy Research and Development Administration (now part of the Department of Energy) in 1975.
***Formerly part of the Health Services and Mental Health Administration.

Table 3. Support Funds of IATC Member Agencies
Fiscal Years 1972 to 1974

	NHLI	Other NIH Institutes	Other IATC Members	Total
		(dollars in millions)		
1972*	$177	$50	$ 81	$308
1973**	132	82	128	342
1974***	253	95	178	526

*DHEW Publication Nos. (NIH) 73-522, 73-523, 73-524.
**DHEW Publication Nos. (NIH) 75-686 and 75-687.
***DHEW Publication Nos. (NIH) 76-1001, 76-1002, and 76-1003.

sponsored by the IATC. In the second volume, the IATC provided for the first time a listing of the projects supported by its member agencies. In fiscal year 1977, there were 7,600 individual projects in cardiovascular, pulmonary, and blood-related research, with funding at $465 million.

Two years later, the IATC published a four-volume report on fiscal year 1979 activities.† Entitled "National Program Coordination," the first volume included a narrative overview of fiscal year 1979 research efforts; the second consisted of listings of projects in heart and blood vessel diseases; the third focused on lung and blood diseases and blood resources; and the fourth contained a compendium of projects related to smoking and heart, lung, and blood diseases. These documents reported on 8,868 projects, funded at a level of $647 million.

WORKING GROUPS

In 1975, the IATC expanded its activities by forming several working groups with responsibilities that include the assessment of the current status of research in particular areas, the identification of areas in special need of interagency collaboration and coordination, and the promotion of information exchange

†NIH Publication Nos. 81-2181, 81-2182, 81-2183, and 81-2184.

on the programmatic rather than policymaking level. The first working groups were on pediatric pulmonary diseases, sickle cell disease education, and high blood pressure control. The IATC subsequently established working groups on cardiovascular biomedical engineering, nutrient composition of foods, program impact analysis, smoking and heart, lung, and blood disease, and blood resources and blood substitutes. Membership of each working group is selected from experts in IATC member agencies. Groups meet regularly to develop approaches to coordination and collaboration in their special fields of research.

Working Group on Pediatric Pulmonary Diseases

The Working Group on Pediatric Pulmonary Diseases was formed to explore the potential for interagency collaboration in programs related to lung disorders. The initial membership included:

- National Heart, Lung, and Blood Institute
- National Institute of Arthritis, Metabolism, and Digestive Diseases (NIAMDD, now the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases)
- National Institute of Child Health and Human Development (NICHD)
- National Institute of Allergy and Infectious Diseases (NIAID)
- Health Services Administration.

This working group initially examined the possibilities of joint sponsorship of a symposium on biology and chemistry of basement membranes; joint sponsorship of projects in cystic fibrosis; information exchange between NHLBI-supported pediatric pulmonary research projects and HSA Maternal and Child Health Service Programs involving crippled children; and information exchange between the NHLBI Pulmonary Specialized Centers of Research and the HSA Pediatric Pulmonary Centers. This examination of the total Federal effort in lung diseases facilitated the cooperative relationships in the areas identified above. The working group also collaborated with the NIH Cystic Fibrosis Coordinating Committee on the development of a program announcement for basic and clinical studies in cystic fibrosis, and it assisted in developing plans for an evaluation of the results of research on pediatric pulmonary disease supported by the Division of Lung Diseases, NHLBI.

In the fall of 1981, the NHLBI recognized the need to expand the coordination effort to the entire lung program, and the

working group was dissolved. It is anticipated that a new working group on Federal pulmonary programs will be established as a new IATC initiative.

Working Group on Sickle Cell Disease Education

The Working Group on Sickle Cell Disease Education was established to:

- Assess the status and needs in the area of sickle cell disease education.
- Identify areas of gap, overlap, and duplication among IATC member organizations.
- Identify areas of interagency collaboration and coordination in sickle cell disease education and information programs.
- Maximize interagency information exchange.

Representatives from the National Institutes of Health, Health Services Administration, Centers for Disease Control, Veterans Administration, Department of Transportation, Department of Defense, Department of Labor, Office of Education, and the Rehabilitation Services Administration participated in this working group. The group initially reviewed sickle cell educational and information programs implemented by Federal agencies. Programs were examined to identify gaps and needs for expansion and coordination. The consensus of the members was that some duplication of agency activities was desirable in view of the variations in the populations that the group served, but that interagency coordination was essential.

As the working group evolved, its focus narrowed to a specific activity involving the Rehabilitation Services Administration, which is mandated by Congress to serve severely handicapped individuals. Because sickle cell disease patients often have physical limitations during the course of their disease and are regarded as handicapped under RSA definitions, they are eligible for rehabilitative services in accordance with state and local regulations. The IATC member from the RSA provided the working group with a report on a model program involving cooperation between a sickle cell center and a local rehabilitation agency that had demonstrated success in rehabilitating a significant population of sickle cell disease patients. Services included physical and occupational therapy, vocational counseling

and training, psychological and social counseling, and job placement. Encouraged by this report and also by data showing limited use of the services of local rehabilitative centers due to lack of followup and communication between center staffs, the working group recommended a collaborative project to increase participation of sickle cell patients in vocational rehabilitation programs. Sickle cell centers were encouraged to promote cooperation by educating counselors in rehabilitation centers about sickle cell disease. Prospective sites for collaboration were identified in areas with sickle cell centers and rehabilitation centers. Federal and state regulations for the provision of vocational rehabilitation services to sickle cell patients were made available to the sickle cell centers, and locations and contacts at the various rehabilitation centers were provided. Information packages were developed with background material on sickle cell disease and on specific needs of sickle cell patients in rehabilitation.

The working group developed a collaborative effort through the sickle cell center network, with the goal of increasing services to sickle cell disease patients. After accomplishing its initial objectives, the group became inactive. Since many of the participating agencies are represented on the national Sickle Cell Disease Advisory Committee, mechanisms still exist for addressing issues of duplication and overlap and for promoting information exchange. A working group with a broader focus on genetic disease, in the context of health promotion and disease prevention, is being considered for the future.

Working Group on High Blood Pressure Control

The Working Group on High Blood Pressure Control was formed to evaluate hypertension control programs at the worksite, using existing Federal employee health programs as models. Representatives from the following agencies have participated:

- Department of Health and Human Services
  - Alcohol, Drug Abuse, and Mental Health Administration
  - Centers for Disease Control
  - Health Resources Administration
  - Health Services Administration
  - National Institutes of Health
  - Rehabilitation Services Administration
  - Social Security Administration

- Other Federal agencies
  - Civil Service Commission
  - Consumer Products Safety Commission
  - Department of Agriculture
  - Department of Commerce
  - Department of Defense
  - Department of Energy
  - Department of Labor
  - Department of Transportation
  - Environmental Protection Agency
  - National Science Foundation
  - National Aeronautics and Space Administration
  - Veterans Administration.

The working group has reviewed and critically analyzed extensive literature related to hypertension at the worksite. The group endorsed the Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure, and suggested that the report be widely distributed and that its recommendations be adopted as basic medical criteria by all government occupational health services. The group has also reviewed employee hypertension programs conducted in various Federal agencies.

As a result of these activities, the Division of Federal Employee Health agreed to review its Manual of Operations for Public Health Service Health Units to assure conformity to the joint committee report where applicable to its programs. The working group has thus facilitated significant improvement in the hypertension control program for Federal employees while pursuing its primary goal of developing an effective approach to screening, educating, and treating hypertensives at the worksite.

In 1979, the working group sponsored a conference on high blood pressure education and control for Federal employees, and the results and recommendations were presented in "Conference on High Blood Pressure Control in the Federal Work Setting." Federal and other public agencies subsequently initiated improved educational programs in this important health area.

The Office of Personnel Management is evaluating a program sponsored by this working group to develop, distribute, and promote materials for Federal and other public agencies to improve education about high blood pressure. A directory of high blood pressure screening and education programs, compiled by the working group with the assistance of the NHLBI, is an important step toward identifying community resources to support employee health units in this education and control effort. The chairman of the working group reported in detail at the September 1980 meeting of the IATC on the potential implications and future directions of

the NHLBI-sponsored National High Blood Pressure Education Program (NHBPEP). National and international groups are now investigating the new criteria for determining hypertensive ranges reported by the NHLBI Hypertension Detection and Followup Program (HDFP). Since under the new criteria, many people have "mild" hypertension, extensive changes are needed in public information and education efforts.

This working group is currently dormant but can be reactivated if future collaborative efforts in hypertension treatment and control are needed.

Working Group on Cardiovascular Biomedical Engineering

Biomedical engineering has increased in importance with the application of theory derived from the physical and engineering sciences to the solution of medical and health care problems. Particular attention has been given by biomedical engineers to cardiovascular research. In response to the need for improved communication and coordination among federally funded programs, the Working Group on Cardiovascular Biomedical Engineering was formed. Its three primary goals are to:

- Encourage Federal agencies to exchange programmatic information through meetings and workshops.
- Examine the state of knowledge to discern problem areas specially suited for interagency collaborative approaches.
- Develop candidate projects for interagency collaboration and make recommendations to the IATC for implementation.

Representatives from the following Federal agencies participated in the first meeting of this working group:

- Department of Agriculture
- Department of Defense
- Department of Transportation
- Department of Energy
- Environmental Protection Agency
- Food and Drug Administration
- Health Resources Administration
- Health Services Administration
- National Aeronautics and Space Administration

- National Institutes of Health
- National Science Foundation
- Veterans Administration.

The working group began by examining and analyzing member agency involvements in cardiovascular biomedical engineering (CVBME). These activities included basic and applied research, the use of CVBME techniques and devices, and the regulation and assessment of such techniques and devices. Working group members suggested several benefits to be derived from increased communications concerning research, use, regulation, and assessment of CVBME techniques, devices, and products. Efforts in these areas include:

- Identifying and evaluating the status of Federal CVBME projects.

- Sponsoring, at a working group meeting, a presentation by the Food and Drug Administration of its procedures for setting standards and for clinical premarketing testing of biomedical devices.

- Examining the expanded mandate of the Environmental Protection Agency and the development of its National Environmental Research Center Human Studies Laboratory to determine the potential implications for CVBME.

These activities have enhanced interagency communications and may lead to the identification of other projects in which interagency collaboration will be desirable.

In exploring new mechanisms for facilitating cardiovascular device research and development, the working group began to focus on particular aspects and problems of device development and transfer by reviewing biomedical engineering issues in the entire biomedical research spectrum. In this capacity, the group's efforts have formed the basis for IATC discussions of technology transfer and assessment. The focus of the group thus far has been on issues involved in development, assessment, and dissemination of information on pacemakers, noninvasive diagnosis and evaluation methods, heart valves, ambulatory monitoring, and the left ventricular assist device. Other specific areas of interest include:

- The progress of a collaborative clinical program to validate the measurement variability of B-scan ultrasonic imaging systems compared to intra-arterial arteriography in patients with carotid and ilial-femoral disease.

- Digital subtraction angiography as a cost-effective and useful diagnostic tool.

- The results of a collaborative study, done by the National Aeronautics and Space Administration and the NHLBI, in which a technology developed at the NASA for ion-sputtering of metals, ceramics, and plastics was applied to a pumping bladder of a heart assist device to determine the optimum surface texture.

The working group has also been concerned with areas of pacemaker technology of interest to the FDA, National Bureau of Standards, VA, and NHLBI. Questions of concern have addressed regulations, modes of failure, and other problems. The group has reviewed the experience of the FDA, the VA, and European pacemaker registries as sources of basic information about pacemaker failures and actuarial survival rates, and about the detection of mechanisms of failure.

In the future, this working group will address such needs as improving relations between Federal agencies and private research organizations, assessing patent rights in device development and the costs of device development and transfer, developing methods for collecting data on success or failure of devices, and encouraging device promulgation. The group is also considering activity in preparing guidelines and standards for monitoring device development.

Nutrient Data Research Working Group

For many years, the NHLBI cooperated with the Department of Agriculture and the Food and Drug Administration in projects related to the nutrient composition of foods, with the hope that appropriate modification of the nutrient content of the food supply would help ameliorate cardiovascular disease. Because of the importance of the subject, other Federal organizations were invited in 1976 to join in the formation of a working group. The Working Group on Nutrient Composition of Foods, as it was initially named, was established to address issues of mutual agency concern related to the nutrient composition of foods in the U.S. diet and its relationship to heart, blood vessel, lung, and blood diseases. Representatives from the following agencies attended the initial meeting:

- National Heart, Lung, and Blood Institute

- Administration on Aging (Department of Health, Education, and Welfare)

- Department of Defense

- Department of Agriculture
- Environmental Protection Agency
- Food and Drug Administration
- Health Services Administration
- National Aeronautics and Space Administration
- Veterans Administration.

The working group discussed interagency needs for:

- An adequate methodology for routine analysis of food components.
- A system to monitor the nutrient composition of newly developed food products.
- Improved research methodology to obtain an understanding of dietary interactions and of the bioavailability of nutrients as they are consumed in food.
- An understanding of the effect of food processing on nutrient content.
- Basic food composition data for use in research, patient education, public education, food labeling, and food purchasing by hospital food services.
- Reliable data on the effects of diet on health, for use in public education to improve dietary patterns.
- Exchange of information among agencies supporting research-oriented activities and agencies involved with health care delivery.

In 1979, the working group formed a special subgroup to develop a rationale and mechanisms for establishing cardiovascular research priorities in the analysis of nutrient composition of foods. The subgroup included representatives from the working group, other Federal agencies, researchers, medical practitioners, and industry. The working group used the recommendations of the subgroup to coordinate the efforts of the member agencies in developing nutrition guidelines related to treatment and prevention of cardiovascular diseases.

The working group examined interagency collaboration in connection with the USDA nutrient composition research program. The group also considered the relevance of two NHLBI studies to

IATC member agencies: the investigation of the relationship between nutrition and levels of high density lipoproteins, and the dietary intake findings from the Lipid Research Clinics Prevalence Study.

Interagency cooperation with the USDA has included joint support by the NHLBI and the USDA of a comprehensive literature search to update data on fatty acids and cholesterol in foods. A nutrient data base is also currently maintained at the Nutrient Coding Center in Minneapolis. Another area of collaboration has been the establishment and continued joint support of the USDA Nutrient Composition Laboratory, where data have been compiled from analyses of the most frequently consumed foods in the United States. In addition, the NHLBI and the USDA are attempting to develop a "typology of eaters" based on consumption patterns of food groups, with the goal of determining if it is feasible to develop different guidelines to suit various eating behaviors.

In 1982, this working group was superseded by the Nutrient Data Research Working Group. The new group focuses more specifically on:

- The goals of the Nutrient Coding Center and the interagency agreements between the USDA and the NHLBI.
- Planning for additional collaborative agreements with the Nutrient Composition Laboratory and the Consumer Nutrition Center, USDA.
- Identification of gaps in data on nutrient composition of foods.
- Establishment of priorities in nutrient data composition.
- Recommendations of appropriate future directions for the Nutrient Composition Laboratory with regard to the needs of the NHLBI.

Initial interagency representation on the new working group includes, in addition to the NHLBI, the USDA Health and Nutrition Survey and, as ex officio members, the Centers for Disease Control, the National Center for Health Statistics Health and Nutrition Survey (HANES), and the Food and Drug Administration.

Working Group on Program Impact Analysis

The Working Group on Program Impact Analysis was created in response to the need for consistent baseline data on morbidity, mortality, and the impact of technology on the health care system. These data are necessary for the evaluation of programs on disease

and health problems and for making program decisions. Current mortality indices and calculations of the economic costs of cardiovascular, respiratory, and blood diseases do not adequately reflect the effects of individual programs either on particular diseases or on health problems. A purpose for the establishment of this group was to develop a comprehensive set of measures to evaluate the effects of programs.

Agencies represented on this working group included the:

- Centers for Disease Control
- Department of Transportation
- Energy Research and Development Administration
- Environmental Protection Agency
- Food and Drug Administration
- Health Resources Administration
- Health Services Administration
- National Aeronautics and Space Administration
- Division of Heart and Vascular Diseases and Office of Program Planning and Evaluation, NHLBI
- Rehabilitation Services Administration
- Veterans Administration.

The working group served as a focal point to facilitate collaborative efforts among the IATC member agencies. It identified relevant data bases and sources in the Federal Government, identified data needs of member agencies, and discussed means of using the available data on cardiovascular and pulmonary diseases, including studies of trends in various risk factors. The group also considered approaches to identifying changes in risk factors and patterns of care that could be associated with the continuing decline in coronary heart disease mortality.

This group is now inactive. It may be replaced by a new working group to address the growing importance of the transfer of technologies into clinical practice.

Working Group on Smoking and Heart, Lung, and Blood Diseases

The Working Group on Smoking and Heart, Lung, and Blood Diseases, formed in 1979, is different from other Federal smoking-related programs because of its interagency coordinative and collaborative focus. Its goal is "to coordinate those aspects of Federal programs that are directed at reducing the morbidity and mortality associated with heart, lung, and blood diseases caused or exacerbated by smoking."

The membership of this group includes:

- Centers for Disease Control
- Department of Agriculture
- Department of the Army
- Department of Energy
- Office of Smoking and Health, HHS
- Environmental Protection Agency
- Health Services Administration
- National Aeronautics and Space Administration
- National Cancer Institute
- Division of Heart and Vascular Diseases and the Division of Lung Diseases, NHLBI
- National Institute on Handicapped Research
- Office of Personnel Management.

The group has explored a variety of approaches to programs to stop smoking. It serves as a review committee for the Comprehensive Quit Smoking Community Intervention Plan, which is a project that uses television marketing techniques, newspaper advertising, and assistance from local chapters of the American Lung Association to teach the skills needed to quit smoking. The group is also coordinating the development of a pilot continuing education workshop for Federal physicians to teach them counseling skills that will help their patients quit smoking.

The working group has also initiated a project to evaluate antismoking policies in the Federal workplace. The group selected an organization to design the evaluation instrument and to conduct a survey among Federal workers in the Washington, D.C., area. The

results of this assessment should prove useful in determining the impact of antismoking policies on smoking in the Federal workplace, and will permit development of model standards for policies on smoking in Federal and non-Federal work settings.

To foster the exchange of program information, the working group developed a compendium of research projects related to smoking and heart, blood vessel, lung, and blood diseases. The compendium is presented as volume 4* of the IATC report for fiscal year 1979, and will be updated periodically. This group has also formed a biomedical-biochemical sciences subgroup to identify and exchange information on research issues and resources.

Agendas for the meetings of the working group often include topics intended as continuing education for its members. The group, for example, has discussed carbon monoxide released as a result of smoking and its relationship to heart, blood vessel, lung, and blood diseases, and has investigated possible opportunities for interagency collaboration in this area.

Working Group on Blood Resources and Blood Substitutes

The Working Group on Blood Resources and Blood Substitutes was organized in 1981 to examine and coordinate Federal research on blood and blood substitutes designed to reduce disability, morbidity, and mortality from diseases or conditions for which whole blood, its components, or substitutes provide preventive or curative treatment.

Federal agencies represented on the group include:

- Centers for Disease Control
- Department of Defense
- Division of Research Resources, NIH
- Federal Emergency Management Agency
- Food and Drug Administration
- Health Services Administration
- National Aeronautics and Space Administration
- National Cancer Institute
- National Center for Health Services Research
- National Center for Health Statistics

*NIH Publication No. 81-2184.

- National Institute of Allergy and Infectious Diseases
- National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases
- National Institute of Child Health and Human Development
- National Institute of General Medical Sciences
- National Institute of Neurological and Communicative Disorders and Stroke
- National Library of Medicine
- National Science Foundation
- Rehabilitation Services Administration
- Veterans Administration.

In addition to this representation, the working group includes official observers from private organizations active in the areas of blood resources and blood substitutes, including:

- American Association of Blood Banks
- American Blood Commission
- American Blood Resources Association
- American Red Cross
- Autotransfusion Study Group
- Council of Community Blood Centers
- Institute of Medicine, National Academy of Sciences
- National Research Council, National Academy of Sciences
- National Hemophilia Foundation.

The working group meets four times a year. Major scientific presentations are made on such topics as apheresis, autotransfusion, blood substitutes, compatibility testing, blood components and new products, resource management, and specific disease problems related to blood transfusion, such as viral hepatitis.

The major focus of the working group is on past, present, and future research, not on policy or management of blood resources. The group is compiling a compendium of blood resources research being undertaken by the public and private sectors. The group has also reviewed past and present nationwide blood-related research and has identified areas holding greatest promise or needing closest attention in the immediate future. The group plans to

publish a scientific report for the national biomedical community on problems in blood resources and blood substitutes.

Frequently, experts in areas specifically related to blood resources and blood substitutes are invited from throughout the United States and Canada to working group meetings to present advances in research and to discuss problem areas. These interchanges provide opportunities not only for information exchange between the many federally supported and private organizations responsible for blood resources research and management, but also for the identification of areas where joint research efforts can be initiated and scarce funding conserved.

In the future, areas of research on new blood substitutes, resources, and technologies will be explored. Technology transfer will be implemented, such as therapeutic apheresis.

Importance of the Interagency Technical Committee

The Interagency Technical Committee on Heart, Blood Vessel, Lung, and Blood Diseases and Blood Resources is one of several interagency committees mandated by the Congress to prevent duplication of effort by different agencies working in the same disease areas. As funding for biomedical and other types of scientific research becomes scarcer, it is clearly to the advantage of all Federal agencies to avoid the funding of identical research projects at several institutions when a single, coordinated effort would not only result in fiscal savings but would also be likely to lead to speedier results.

All of the committees responsible for coordinating Federal research efforts share one basic concern--how best to achieve research goals. In addition to organizing the working groups, the IATC encourages exchanges of information among its member agencies by scheduling, at committee meetings, individual agency presentations of specific areas of important research. The discussions frequently lead to suggestions for more concrete collaborative efforts. An agency, for example, might report on research that has led to substantial advances in a given area of cardiovascular, respiratory, or blood diseases; another might present difficult and unanticipated problems in some fundamental investigations. In addition, discussions of specific program topics at IATC meetings provide opportunities for program managers within the agencies to interact, to obtain different points of view, and to suggest research where known deficiencies exist. When an agency determines that a new initiative should be undertaken, opportunities exist for interagency collaboration such as joint program announcements, interagency collaborative agreements, and joint funding. In cases where overlap is demonstrated, suggestions can

be made that might eliminate such duplication and refocus emphasis, so that agencies have different but complementary approaches.

Working groups that have lost their relevance are discontinued or redirected to more current areas of activity. The Working Groups on Pediatric Pulmonary Diseases, Sickle Cell Disease Education, and Program Impact Analysis, for example, all achieved their original goals and were discontinued or deactivated. The Working Group on Nutrient Composition of Foods was dissolved, and the Nutrient Data Research Working Group was formed with a different focus and goals. The IATC also seeks opportunities to establish new working groups in cardiovascular, pulmonary, and blood research areas that show potential for major scientific advances in the future, particularly as complex and sophisticated technologies become more abundant and problems emerge that will benefit from interagency expertise. One example of such an area is the question of alanine aminotransferase (ALT) testing for non-A,non-B hepatitis, which is currently being addressed by the Working Group on Blood Resources and Blood Substitutes.

Trans-NIH Areas

Because many diseases, disciplines, research tools, and research resources extend beyond the purview of any single NIH institute, special mechanisms are needed to ensure the coordination of efforts within and outside the NIH. In 1977, the Director of the NIH identified six such areas for special consideration as "trans-NIH health problems": cystic fibrosis, diabetes, arthritis, genetic diseases, nutrition, and epidemiology. The Director established a coordinating committee for each of these areas to:

- Provide a focus for the exchange of information at the NIH.
- Strengthen and improve the NIH system for reporting on research and related activities in these special interest areas.
- Provide a focus to stimulate research in the areas.
- Encourage joint sponsorship of workshops, conferences, and symposia.
- Explore opportunities to promote the sharing of facilities and other resources among the institutes and divisions.

- Facilitate collaboration in the development of joint programs.

- Coordinate these efforts with other Federal agencies.

During the annual research planning cycle, the Director of the NIH meets with the chairmen and members of coordinating committees to review progress, discuss issues, and assess plans for future activities. The areas selected each year vary as research needs change. Although formal annual review of each area may not be necessary, ongoing monitoring assures that special attention is directed to the areas of greatest concern, and it avoids the institutionalization of formal reporting requirements. The areas not selected for formal review are covered by the appropriate committees, and reporting requirements are met through less formal mechanisms.

The trans-NIH coordinating committees meet regularly and publish annual reports on coordinated research efforts of the previous fiscal year. Agendas of the meetings vary. Several institute or agency representatives, for instance, might lead discussions of a single topic, or one agency might present several research projects being undertaken in a particular trans-NIH area. This exchange of information increases the knowledge that each institute has about the research interests of other institutes and also reveals areas in need of further study. Ideas for new approaches to achieving a better understanding of the fundamental causes of many of the diseases of the heart, blood vessels, lungs, and blood also emerge.

The NIH continues to encourage trans-NIH coordination. As research needs change, coordinating committees can be disbanded, emphases can be revised, new issues can be added, and new committees can be established.

In addition to these trans-NIH issues, the NHLBI developed in 1978 a system for reporting many topics that have trans-NIH implications, such as prevention, smoking and health, digestive diseases, drug abuse, aging, alcohol-related research, behavioral research, environmental research, hypertension research and education, pediatrics, and toxicology. At a program level within the NHLBI, each research project is scrutinized carefully for possible trans-NIH relevance and is entered into a central data base as a percentage of the total project applicable to the particular trans-NIH topic. In this way, coordination between the NHLBI and other institutes of the NIH and other Federal agencies is facilitated, areas where overlap or duplication might be occurring become apparent, and opportunities for collaboration emerge. With the increasing scarcity of funding for health research, joint efforts can lead to the support of research projects that might not receive financing from a single agency

because of their costliness. In addition, research objectives can often be achieved more quickly through a joint effort.

Other Areas

The NHLBI has a long history of joint endeavors with other institutes of the NIH and with other Federal agencies, such as the development of a controlled trial in clinical diabetes, the creation of packaged curriculum materials for training primary care providers in patient education, the evaluation of a national training course for emergency medical technicians, and a study of the adequacy of the supply of blood coagulation factors needed by hemophiliacs. Interagency efforts often take the form of task forces and workshops that bring together scientific and professional representatives from Federal agencies and nongovernment organizations with responsibilities for the conduct or support of basic research and health care delivery. Such groups have critically examined health issues such as hemophilia, cystic fibrosis, respiratory diseases, heart diseases in childhood, blood plasma fractionation, and hypertension. They also strive to promote cooperation and avoid duplication of effort.

Formal interagency agreements with many Federal agencies have been an integral part of the NHLBI's collaborative efforts to support research in the National Program areas. In 1977, for example, cooperative agreements existed with the following agencies:

- Centers for Disease Control
- Department of Agriculture
- Department of Energy
- Department of Transportation
- Environmental Protection Agency
- Food and Drug Administration
- Health Services Administration
- National Aeronautics and Space Administration
- National Bureau of Standards
- Public Health Service
- Veterans Administration.

Formal agreements have been used for such diverse efforts as:

- Testing in a joint project with the Veterans Administration the efficacy and safety of propranolol as an antihypertensive agent.

- Developing, with the USDA, national food composition tables.

- Supporting, in cooperation with the HSA and the CDC, a national network of Sickle Cell Screening and Education Clinics.

- Providing jointly with the CDC coordinated uniform laboratory standards and quality control for major NHLBI-supported clinical trials.

- Testing, in cooperation with the National Bureau of Standards, newly developed biomaterials.

- Providing support with the FDA for the operation of the Blood Establishment Inspection and Registration System.

- Developing with the National Institute for Occupational Safety and Health, the FDA, and the EPA an international satellite-linked computer-based chemical information system.

- Conducting an epidemiological research project with the ministries of agriculture in Finland and in Italy and with the USDA to correlate the effects of dietary fats with platelet function and platelet and plasma lipid composition in humans.

- Cosponsoring with the Department of Transportation a study to analyze the effects of emergency medical systems on prehospital emergency cardiovascular care.

- Undertaking with the Department of Energy an evaluation study of the relationship between antecedent risk factors and atherosclerosis, using autopsy data from victims of coronary heart disease and stroke in Japan.

- Conducting with the EPA, the National Center for Health Statistics, and the National Bureau of Standards an epidemiological study of the relationship between examined cardiovascular measurements and bulk and trace elements such as copper, zinc, cadmium, and lead found in some tap water.

- Working with the VA to develop a noninvasive method for detecting pulmonary emboli.

- Conducting with the HSA an evaluation study of five high blood pressure control demonstration projects in community health centers.

The NHLBI will continue to enter into formal interagency collaborative efforts whenever there is an opportunity to acquire scientific information that will provide better means to prevent, diagnose, and treat cardiovascular, pulmonary, and blood-related diseases.

2. Prevention, Education, and Control

Contents

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The National Heart, Blood Vessel, Lung, and Blood Act of 1972 (P.L. 92-423) gave the Institute responsibilities for "investigation into the epidemiology, etiology, and prevention of all forms and aspects of heart, blood vessel, lung, and blood diseases, including investigations into the social, environmental, behavioral, nutritional, biological, and genetic determinants and influences involved in the epidemiology, etiology, and prevention of such diseases."

To that end, Dr. Theodore Cooper, the Director of the Institute, in the National Program mandated by the act and submitted to Congress in May 1973, outlined a series of goals in prevention, control, and education relating to the disease entities of concern to the Institute. It was recognized even then that "prevention will require local community and regional participation in the control of . . .diseases." This statement has proven prophetic over the years.

The act of 1972 also specified that cooperative programs be established with non-Federal health agencies for the purpose of controlling and, in the long run, preventing diseases of the heart, blood vessels, lungs, and blood. With this goal in mind, the National Heart and Lung Advisory Council recommended the development of demonstration projects to test education methods and to guide community and regional efforts to detect, diagnose, and treat these diseases and establish rehabilitation programs. These programs were to be disease-specific and were to be conducted in cooperation with existing local health resources to facilitate the transition from Federal support of demonstration projects to local control of the diseases.

To implement the Institute's prevention, education, and control programs, the Office of Prevention, Education, and Control (OPEC) was established in 1974. The office is charged with planning, coordinating, and developing Institute policies and programs in the areas of information and education; developing educational and informational materials for use by health professionals in the prevention, diagnosis, and treatment of diseases, and for use by the public in gaining a better awareness and understanding of these diseases; transferring knowledge gained through research into clinical practice through educational measures, demonstrations, and other means; stimulating disease prevention and health promotion activities in a number of settings

including health care setting, schools, the workplace, industry, and the community; and administering an information center to disseminate scientific, technical, and public information.

Disseminating information about research activities of the National Heart, Lung, and Blood Institute is one of the major tasks of the OPEC. Since the creation of the Institute in 1948, great importance has been placed on translating the results of research and disseminating the results of clinical trials to professionals and the lay public. In performing this function, the OPEC sponsors press conferences, issues press releases, develops brochures, pamphlets, and fact sheets, and displays exhibits at appropriate meetings.

Among its earliest efforts, the OPEC helped foster the formation of the professional association for the directors of continuing medical education of American medical schools. Also through OPEC influence, a task force of the Association of American Medical Colleges created a medical school training program in response to the demand for continuing medical education, and it also developed a model medical practice act to link licensure to competence.

In the First Annual Report of the Director, NHLBI, Dr. Cooper discussed the diseases of primary importance to the Institute, the major avenues along which prevention activities were to be directed, the specific programs to be undertaken, and the initiation of what later became the significant clinical trials of the decade. The two areas of particular emphasis were hypertension and arteriosclerosis, for which some prevention activities were already under way.

The National High Blood Pressure Education Program was launched in 1972 to combat a disease that afflicted millions of Americans, 49 percent of whom were unaware of their disease. Only one-eighth of hypertensive patients were under effective treatment in 1972, and the cost to the Nation in lost productivity, wages, and medical care for high blood pressure was estimated at $8 billion. Basically, the NHBPEP was to stimulate better high blood pressure control by informing and educating the public and the medical profession about the serious health consequences of high blood pressure and about the benefits associated with its effective control.

Knowledge of the causes, treatment, sequelae, and prevention of hypertension was sparse at the time the program was established. As late as 1950, hypertension was usually diagnosed only when the patient exhibited some of the serious clinical effects of the disease. Treatment consisted of drugs that had serious side effects and of the so-called rice diet, which was unpalatable to some and only modestly effective. It was not until the late

1960's and early 1970's, after completion of several clinical trials, that the benefits of controlling high blood pressure were demonstrated. Many questions, however, remained unanswered. The clinical trials that had been undertaken demonstrated that drug therapy was effective in controlling moderate and severe high blood pressure in males but did not indicate whether the same was true for women, minorities, and the community at large, or for individuals who had "mild" hypertension. Thus, the stage was set for establishing a program that would launch a national effort to lower the morbidity and mortality from this widespread disease.

The genesis of the NHBPEP actually preceded by a few months the congressional mandate for the Institute's activities in prevention, education, and control. The NHBPEP was established by Elliot Richardson, Secretary of Health, Education, and Welfare, who designated the Institute as the coordinating agency for the initiative. Early guidance and advice were provided by a chartered public advisory group, by the Hypertension Information and Education Advisory Committee (HIEAC), and by an ad hoc liaison group of Federal agencies, the Interagency Working Group. An additional group, the Program Resource Group, was formed in late 1973.

After the three advisory committees were disbanded in 1974, the Institute formed the National High Blood Pressure Coordinating Committee in 1975. This advisory body remains in force today. Originally comprised of representatives of the eight signatory sponsoring groups for the first National High Blood Pressure Month, the committee has grown over the years to 30 participating organizations.

The NHBPEP became a successful program, for it exerted a significant positive effect on the problem of high blood pressure among the population, with a comparatively low investment of Federal funds. Program directors confined the government function to that of coordination to provide selected government resources to complement the resources of private health care organizations, which in turn enhanced their own health care delivery efforts.

In 1974, the President declared May to be High Blood Pressure Month, and he brought the subject into special public focus and attention. The NHBPEP provided materials, assistance, and "month kits" to help local programs, often in conjunction with local media, bring the information to the public in a more effective manner. Additional educational messages were provided directly to the media by the Institute and by the organizations on the coordinating committee.

The results of two public polls taken 6 years apart (1973 and 1979) showed that these efforts were having a significant positive impact on the public perception of the problem of hypertension.

In 1973, 57 percent of those interviewed recognized high blood pressure as a "very serious disease" and 77 percent said that they had had their blood pressure measured within the past 12 months. By 1979, 73 percent recognized high blood pressure as a very serious disease and 83 percent had had their blood pressure measured. In addition, 89 percent of those interviewed in 1979 were aware that high blood pressure could exist without overt symptoms, and 93 percent knew that high blood pressure could be treated effectively.

There are also some indirect measures of the effectiveness of the NHBPEP. The number of articles appearing in the lay press increased both in quantity and accuracy, and the number of patient visits to physicians for treatment of high blood pressure increased. In addition, there was a change in prescribing patterns of physicians, who now treated high blood pressure more often and more effectively, and there were more articles in the professional literature on patient treatment for high blood pressure rather than primarily on the basic underlying physiology of the disease.

Between 1971 and 1980, these indications of progress translated into real numbers for hypertension patients. A survey in 1971 revealed that more than 49 percent of persons found to have high blood pressure were unaware that they had it. By 1980, the number of hypertensives unaware that they had the condition had decreased to less than 27 percent. Even more important, the 1971 survey showed that only 16.5 percent of persons with high blood pressure who were taking medication also had their hypertension under control. By 1980, that number had more than doubled to 34.1 percent.

The second major initiative of the Institute's effort against high blood pressure was the initiation in 1972 of the Hypertension Detection and Followup Program, a clinical trial that eventually would involve cooperating medical staffs at 14 clinical centers and nearly 11,000 volunteer participants with high blood pressure. The HDFP attempted to measure the value of treating high blood pressure in mild hypertensives as well as in those with moderate to severe high blood pressure, in women as well as men, and in blacks as well as whites. Results of the HDFP, which were released in late 1979, answered many questions regarding the health benefits of treating hypertension.

At the beginning of the study, 10,940 volunteers, aged 30 to 69, were randomized into two groups: the referred-care (RC) group, who were referred back to their community health care facilities for necessary medical attention, and the stepped-care (SC) group, who underwent a systematic antihypertensive treatment program using drugs in a stepped-care manner within the cooperating clinical centers. The patients were further divided into

three strata based on their diastolic blood pressure at entry into the study: 90 to 104, 105 to 114, and 115 and over.

After a 5-year followup period, the SC group was found to have a 17 percent lower overall mortality rate than the RC group. Even more significant was the report that the death rate among the patients in the lowest stratum of high blood pressure on entry (90 to 104 mm Hg) was 20 percent lower among the SC group. A more detailed examination of the HDFP data on stroke mortality and morbidity combined demonstrated a decline in stroke mortality among the SC group for all age groups and for all strata. Stroke mortality and morbidity was 45 percent less in SC than in RC among those in the highest stratum (115 mm Hg or higher diastolic). White women in the SC group experienced a 30 percent reduction, and participants in the youngest group (30 to 49 years of age at entry) showed a 27 percent decline. The oldest group (60 to 69 years of age at entry) experienced a remarkable 45 percent reduction in stroke mortality and morbidity. Survivors in this group were 65 to 74 years of age by the time the study ended.

Analysis of the HDFP data for patients in the lowest stratum of hypertension (90 to 104 mm Hg diastolic) not on hypertensive treatment at baseline and without apparent end-organ damage at baseline shows a dramatic overall mortality reduction. For all causes, those in the SC group experienced 28.6 percent lower mortality after 5 years than did the RC group. In addition, the patients in the same SC subgroup who had an entry diastolic blood pressure of 90 to 94 mm Hg experienced a 34 percent reduction in mortality after 5 years.

A significant fact about the HDFP is that the trial was not a placebo-based study. The patients who were randomized into the RC group were referred to their usual community medical care upon entry into the study and underwent annual examinations at HDFP clinics throughout the 5 years. For participants in the RC group who were found to have a diastolic blood pressure of 115 mm Hg or higher or who were found to have end-organ damage on entry, special efforts were made to arrange for care by a physician. Having been accepted into a high blood pressure study, having been made aware of their disease, and having been repeatedly urged by medical staff to seek treatment, many patients in the RC group were very likely persuaded to consult their physicians. At entry into the study, 26 percent of the RC group were on antihypertensive drugs. By the end of the 5-year followup period, more than 58 percent of these patients were on drug therapy.

In addition to clinical trials involving the testing of direct intervention methods to lower high blood pressure and prevent heart attacks and stroke, the Institute also supports demonstration and education programs using methods that were successful in clinical trials.

The Cornell University Medical College is conducting a community study to develop, implement, and assess methods to improve the control of blood pressure. Based on previous studies demonstrating that systematic approaches to antihypertensive care yield more satisfactory results than can be obtained through conventional approaches, and that antihypertensive care within the context of a socially cohesive environment encourages long-term adherence to treatment, the Cornell study will evaluate specific strategies in two settings. The first is a controlled trial within the worksite to evaluate the effect of on-site nurse monitoring and followup on blood pressure control. The second is designed to assess among the elderly the effect of the cost of antihypertensive drugs, and the accessibility to them, on blood pressure control. Four senior citizen centers in New York City will provide free antihypertension drugs to residents at the centers or at neighborhood pharmacies. Study results will indicate whether cost and accessibility to drugs influence the attainment of high blood pressure control among this population.

The NHLBI has also initiated projects to assess the value of controlling high blood pressure at the workplace. Industry pays for cardiovascular disease through escalating health insurance costs, decreased productivity, absenteeism, employee replacement and retraining costs, disability claims, and death benefits. The cost to industry of hypertensive disease totals billions of dollars annually, probably 15 to 20 percent of the $80 billion exacted by cardiovascular diseases in general.

Thus, for some years the issue of controlling high blood pressure at the worksite has occupied the interest of industrial leaders and medical professionals. In response to this concern, the Institute sponsored 3-year demonstration projects at selected sites of the Ford Motor Company (through the University of Michigan), Westinghouse Electric Corporation, and the State of Maryland. The primary objective of these three programs was to determine whether high blood pressure control is feasible and effective in the workplace. The decision would be based on changes in health status of the workers at the end of a 24-to-30-month period of study.

The project in the Ford Motor Company was undertaken in four plants in the Detroit area, in which each plant was the subject of a different control plan. Screening procedures at all the sites were identical and consisted of prescreening publicity, education, and convenient on-site facilities. The followup and counseling offered after the initial screen differed from site to site according to the protocol.

Followup at site 1 was minimal and was limited to sending a letter to the physicians of the employees found to have high blood pressure to inform the physicians that a referral had been made.

At site 2, there was moderate followup, which consisted of a similar letter and a semiannual appointment of hypertensive employees with the blood pressure counselor in the plant's medical department. At site 3, there was full followup, which involved both the employee and the physician. Blood pressure counselors contacted each hypertensive employee at least every 6 months and gave special attention to employees whose blood pressure was poorly controlled. Findings were discussed with the employees' physicians. Followup at site 4 consisted of offering on-site treatment of high blood pressure. Workers who chose not to take advantage of this option reverted to a program similar to that given in site 3.

Blood pressure control improved at all four sites, but the average reduction in blood pressure at site 1 was approximately one-half that achieved at the other three sites. No workers at sites 2, 3, and 4 dropped out of the program. This datum indicates that even minimal followup is effective in achieving and maintaining adherence. Moreover, absenteeism in these three plants decreased during the 2 years of followup but increased in site 1.

The demonstration program with the Westinghouse Electric Corporation also involved four plants: two in Pennsylvania and one each in New York and California. Again, a prescreening publicity and education campaign started the project, after which, employee screening was begun. Upon completion of the initial screening, followup for employees referred for diagnosis and treatment consisted of letters and questionnaires sent to the employees and their physicians, and of telephone contacts with the employees. The telephone followups varied in intensity at different sites. At site 1, employees were contacted more than once if they failed to return the questionnaires. At sites 2 and 3, there was moderate followup, with only one telephone contact with the employee. A strike at site 4 interfered with telephone contacts and caused employees to be unreceptive. A second mailing was sent if the telephone calls were unsuccessful.

Followup visits by employees showed that blood pressure control had improved at all four sites, but final results at the conclusion of the project were available only for sites 2 and 4. Control rates were similar at these two sites and had been somewhat higher for these sites than at sites 1 and 3. These differences perhaps indicated the value of more frequent counseling.

The Maryland State Government project, which was conducted through the University of Maryland, involved employees at only one site, and they received periodic screening, referral, and followup services. Most of the employees who were identified as hypertensive were treated by their own physicians, but an on-site

clinic was established to offer treatment to employees who chose not to accept referral to community care facilities.

Blood pressure measurements were taken at 6-month intervals, with final measurements at the end of the 24-month period. At that time, 68 percent of the hypertensive employees had adequate control of their blood pressure--a decrease from the peak control of 80 percent measured at the 18-month mark. Researchers were of the opinion that the project's pending termination may have influenced motivation to remain on treatment. Investigators concluded that even though on-site care is not necessary to produce desired results, on-site reinforcement of community care produced excellent results.

The results of these three worksite demonstration programs indicate that high blood pressure control programs can be effective in controlling employee hypertension. They also appear to be cost-effective to the company and reduce absenteeism among controlled hypertensives. Such programs are most effective when employees, unions, management, and health care providers work together and when systematic followup, ongoing counseling, and support are in place.

The benefits of lowered health care costs are of interest not only to industry but also to the health insurance carrier. To demonstrate the value of worksite high blood pressure control programs, the National Blue Cross-Blue Shield Association, in collaboration with the NHLBI, recently completed a 2-year demonstration project on the health insurers' roles in the design and implementation of worksite-based high blood pressure control programs. The objectives were to design and demonstrate a pilot program to train health insurance representatives to market and service worksite control programs; to develop methods and materials to allow the association's divisions to make community high blood pressure control services more available and more accessible; and, pending a successful outcome of the project, to prepare a strategy for a national program to be implemented among the Blue Cross-Blue Shield plans.

The program was initiated in October 1977 and concluded in January 1980. During that time, five blood pressure control pilot programs were initiated: in Connecticut, for Blue Cross employees, a large public utility firm, and a manufacturer; and in Michigan, for a Federal facility and a commercial bakery. Concerted efforts were made to solicit the participation of employees of these agencies, including multimedia publicity campaigns and information materials from the American Red Cross and other sources. Occupational health nurses were trained to provide referral, followup, and long-term monitoring functions.

At the conclusion of the pilot programs, 50 to 80 percent of patients referred to physicians had complied with the referral, and of this group, between 60 and 80 percent were making acceptable progress toward attaining goal blood pressure. Thus, the worker health program model was effective. It demonstrated the feasibility of attaining satisfactory control rates in the programs that were initiated.

To achieve the desired control rates, it was necessary to obtain high rates of participation among the eligible employees. To that end, the program involved an aggressive publicity campaign, a careful scheduling of people to be screened to avoid undue waiting times, visible support from corporate management, and screening facilities in easily accessible locations. It was concluded from the results of this program that health insurers can assume important functions in organizing community resources for workplace blood pressure control programs, in marketing the plans to corporate management, and in assisting employers in the implementation of such programs.

In another demonstration effort, seven centers across the United States are participating in a study of the level of coordination among blood pressure control agencies. After an initial assessment, a coordinating mechanism will be installed. Later, coordination will again be measured, and also prevalence of high blood pressure and levels of patient awareness before and after the coordination mechanism was in place. In rural areas, other demonstration programs are training persons in the community to monitor hypertension among the population and report patients' status to their physicians. Yet another program attempts to influence attitudes, value judgments, and behavior among 6th-grade students. Educational materials emphasize experimental activities that require the students to confront poor health practices and grapple with the consequences.

The Institute's prevention programs were not confined to hypertension awareness and correction. In 1972, the knowledge existed to allow the identification of persons at increased risk of developing heart disease or stroke. Screening to measure blood lipids, blood pressure, and body weight, and obtaining information on smoking would identify the 20 percent of the population that would be most likely to have 40 percent of the heart attacks and 50 percent of the strokes over a 6-year period. Theoretically, once the individuals were identified, measures could be taken to reduce their risk by dietary or drug intervention to lower blood lipids and blood pressure and to encourage them to stop smoking.

To test this concept, two programs in addition to the HDFP were initiated. One was the Multiple Risk Factor Intervention Trial (MRFIT), in which the participants were a group of men who were at risk of death from coronary heart disease because of

elevated blood cholesterol, high blood pressure, or cigarette smoking. The purpose of the MRFIT was to determine whether a special intervention program to lower serum cholesterol, reduce blood pressure, and eliminate or reduce smoking would reduce mortality from coronary heart disease.

Designed to test the effect of special intervention to reduce risk factors, the MRFIT enrolled 12,866 men between 35 and 57 years of age who were considered to be at high risk for CHD because of the presence of one or more risk factors--high blood pressure, high blood cholesterol, or cigarette smoking. The men were entered into the study if they had a diastolic blood pressure of at least 90 mm Hg or were on antihypertension medication, smoked cigarettes, or had blood cholesterol levels that in combination with other risk factors placed them in the upper 10 percent of a risk score distribution.

The participants were randomized into either the usual-care (UC) group (the members were not offered special treatment or counseling, but were referred to community medical care) or the special-intervention (SI) group (the members entered an intensive, specialized program designed to reduce risk factors). Special counseling on nutrition was focused on altering lifestyle habits to lower body weight and reduce blood cholesterol levels and to encourage the development of lifelong patterns of shopping, cooking, and eating to maintain desired cholesterol levels. Treatment was offered for high blood pressure, beginning with weight reduction and progressing to drug therapy if needed. Antismoking techniques were employed throughout the trial, and hypnosis was sometimes used late in the trial for smokers who were especially resistant to quitting. Behavior-modification techniques also were used in special instances in the final years.

At 1-year intervals, the participants in both the UC and the SI groups were seen in the clinics for evaluation. All participants were followed for a minimum of 6 years, and mortality status was determined for all participants.

At the conclusion of the study, mortality in the SI group from coronary heart disease was 7 percent less than that in the UC group. Although the mortality difference between the SI and UC groups was not considered statistically significant, both groups reduced the risk factors more than had originally been projected, and both groups had lower mortality rates than was anticipated. This observation has prompted many to cite the MRFIT findings as further evidence supporting the benefits of risk factor reduction.

The other program, the Coronary Primary Prevention Trial (CPPT) initiated through the Lipid Research Clinics, was to determine whether reducing serum cholesterol by drug therapy could lower the mortality from atherosclerotic coronary heart disease

among men who had hypercholesterolemia but were otherwise healthy. The study is in its closing phases, and results are scheduled for release in 1984.

A comparable program in the Division of Intramural Research was initiated also in 1972. In the Type II Coronary Intervention Study, a small group of patients with type II hyperlipidemia was enrolled to investigate the benefits of lowering serum cholesterol with the use of cholestyramine. Long-term followup is planned to determine whether the drug will result in the regression or arrest of coronary artery disease. The program is still under way.

In addition to the clinical trials on primary prevention (MRFIT and CPPT), the Institute has also investigated efforts in secondary prevention. Among these was the Beta-Blocker Heart Attack Trial (BHAT), which was designed to investigate the efficacy of the beta-blocker drug, propranolol, in preventing mortality among patients who had experienced at least one myocardial infarction. Based on the recommendation of the National Heart, Lung, and Blood Advisory Council, the BHAT, which was initiated in 1977, was scheduled as a 7-year clinical trial.

The study was a randomized, double-blind, placebo trial conducted in 31 clinical centers in the United States and Canada. Men and women between the ages of 30 and 69 who had experienced a heart attack at least 5 days but no more than 21 days before entry into the study were enrolled and randomized into treatment and placebo groups. Patients in the treatment group received either 180 or 240 mg of propranolol per day, and patients in the placebo group received inert pills indistinguishable from the propranolol. In 27 months, 3,837 patients were accepted into the study, all of whom had been followed for at least 12 months when the study ended.

An independent Policy and Data Monitoring Board made up of experts not involved in the study met twice a year to review the status of the trial and examine the accumulated data. The function of the board was to terminate the trial in the event extreme benefit or extreme toxicity of the drug appeared before the scheduled completion. Evidence indicated that the propranolol therapy was showing a statistically significant beneficial effect in preventing mortality, and the board recommended that the trial be suspended so that the results could be released to the medical community. Analysis of the results of the trial indicated that of the 1,921 patients assigned to the placebo group, 9.5 percent died during the followup period. Of the 1,916 in the propranolol group, 7.0 percent died. The difference in mortality between the two groups was 26 percent.

The implications of these findings are substantial. Of the 350,000 patients discharged alive from hospitals every year

following a myocardial infarction, perhaps two-thirds are qualified for beta-blocker therapy. The results in the BHAT trial, based on these figures, show an opportunity to save at least 6,000 lives every year in the United States.

In keeping with its mandate, the Institute has initiated a major prevention program for diseases of the respiratory system. The importance of such diseases is reflected in the fact that more workdays are lost from these conditions than from any other category of illness. Although some workers, such as those in textile mills and coal mines, are at high risk of developing a respiratory disease resulting from the inhalation of particles of matter in the work area, probably the most insidious influence on the development of respiratory disease is cigarette smoking.

Cigarette smoking is the single most important risk factor for chronic obstructive lung diseases, such as chronic bronchitis and emphysema. It also increases vulnerability to acute upper and lower respiratory infections, and a history of frequent acute respiratory infections may well predispose an individual to the development of chronic obstructive lung disease later in life.

Among the epidemiologic evidence supporting the direct link between cigarette smoking and respiratory diseases is that derived from the Tecumseh Community Health Study, an NHLBI-supported program started in 1959. The investigators found that four factors--the subjects' age, sex, smoking habits, and vital capacity (a measure of lung volume)--could identify most of the men and women in the top 10 percent of the risk distribution for the development of emphysema. According to the results of this study, a 45-year-old subject who did not smoke and who had normal vital capacity had only 1 chance in 200 of developing chronic obstructive lung disease during the next 15 years. However, a person of similar age who smoked two packs of cigarettes a day and whose vital capacity was 80 percent of normal increased his or her risk to 1 chance in 5 or 6 of contracting lung disease. The same person could reduce the risk to 1 chance in 15 by stopping cigarette smoking.

Another harmful effect of smoking is that it reduces the effectiveness of the mucociliary mechanisms that clear the airways and lungs of particulate matter, such as bacteria, and of excess mucous secretions. Because these excess secretions may provide a good breeding ground for bacterial invaders, the inadequate clearance of inhaled particulates in smokers increases their vulnerability to lung diseases that result from exposure to infections, organisms, toxic dusts, and allergens. The various forms of asthma associated with the worksite occur with higher frequency and are usually more severe among smokers than among nonsmokers who are exposed to similar workplace environments.

The attempt by smokers to circumvent respiratory diseases by using the so-called less-hazardous, low-tar cigarettes may have reduced the hazard of lung cancer, but for other respiratory diseases the effects have been ambiguous at best. Smokers of low-tar cigarettes still exhibit the decline in pulmonary function seen in other smokers. Thus, quitting smoking is the most effective way to remove the hazards associated with this habit. The "less-hazardous" cigarettes do not seem less hazardous in their influence on respiratory diseases.

Among the respiratory diseases, emphysema and chronic bronchitis have been singled out as being the primary undesirable products of cigarette smoking. Studies had shown that cigarette smokers are far more likely to develop emphysema or chronic bronchitis than are nonsmokers, and once developed, the disease progresses much more rapidly in smokers. Prevention lies obviously in altering the lifestyle of smokers to reduce or stop their consumption of tobacco. To achieve that, the Institute planned programs to modify the habits of smokers and to educate the public about the hazards of smoking and the serious nature of emphysema.

One particular and especially recalcitrant form of emphysema results from a genetic defect that results in reduced levels of alpha-1-antitrypsin in serum, a potent antiprotease that has a protective function in the lungs. Progressive, chronic destruction of the alveoli (the tiny air sacs that constitute most of the lung structure, in which oxygen-carbon dioxide transfer occurs) is the result of an imbalance between the protease and antiprotease within the lungs. Theoretically, the alveoli are constantly exposed to the eroding effects of proteases, particularly the elastase released by the leukocytes. In normal circumstances, alpha-1-antitrypsin builds a powerful antielastase shield that protects the alveoli from destruction.

The protease-antiprotease theory applies both to the hereditary form of emphysema and to that brought on by smoking. NHLBI grantees have found that although smokers may have started with normal protease-antiprotease balance, cigarette smoking deals the lungs a double dose of damage. By impairing the function of the protective alpha-1-antitrypsin, cigarette smoke renders the lung structure more susceptible to attack. Moreover, cigarette smoke activates alveolar macrophages, which in turn attract neutrophils to the lungs. It is these leukocytes that release large amounts of elastase rapidly onto the alveoli. Thus, while the defensive mechanism of the lung is inactivated, the destructive forces are working at an enhanced level.

Obviously, the two avenues of treatment for this condition are to increase the antielastase available to protect the lung or decrease the quantity of elastase within the lung. Researchers have concentrated on attempts to augment the levels of

alpha-1-antitrypsin in deficient individuals. Early attempts consisted of stimulating the liver to produce increased amounts of alpha-1-antitrypsin by the administration of danazol, a modified form of the male hormone testosterone. The hormone itself cannot be safely administered over long periods of time because of pronounced side effects, and it cannot be administered in quantity to women because of its masculinizing effects. Danazol, however, is free of most of these adverse effects, and can be given for long periods of time. In a trial with danazol, NHLBI grantees found that it increased serum alpha-1-antitrypsin by 50 percent in a group of seven patients. Although antielastase levels were not restored to normal levels in these patients, the protease-antiprotease balance was improved and the progression of their lung disease supposedly impeded.

A more direct approach, the parenteral infusion of alpha-1-antitrypsin intravenously, has showed good results in a small group of patients. Purification of the enzyme inhibitor was the initial problem, but scientists supported by the NHLBI developed a comparatively rapid and simple method to partially purify alpha-1-antitrypsin derived from pooled plasma from normal persons. At weekly intervals for 4 weeks, the patients received 4 grams of enriched alpha-1-antitrypsin preparation over a 6-to-8-hour period. Analysis of bronchoalveolar lavage specimens from these patients indicated that the infused alpha-1-antitrypsin reached the alveolar structure. Levels of the protein in serum tested at 70 mg per dL or greater, a level that theoretically could provide protection against elastase within the lower respiratory tract. During this short-term study, none of the patients experienced volume overload, and antibody formation was not detected in reaction to the infused antielastase up to a year after administration.

Long-term studies now are contemplated to determine whether reestablishment of the elastase-antielastase balance will halt the progression of this generally fatal hereditary disease. An estimated 30,000 people in the United States are homozygous for alpha-1-antitrypsin deficiency and are thus at risk of developing progressive, panacinar emphysema. Direct infusion of a given substance has proved valuable as replacement therapy in such hereditary serum protein deficiency diseases as hemophilia, hypogammaglobulinemia, and angioedema.

Another serious respiratory condition is the neonatal respiratory distress syndrome (NRDS), which causes the death of thousands of premature infants. In the United States, approximately 10 percent of infants are born prematurely, and some 50,000 cases of NRDS are reported annually. Hospital stays for these infants average 23 days at a cost of $1,000 a day. The underlying cause of the syndrome is the immaturity of the lungs of the prematurely born. Their lungs are incapable of providing

sufficient respiratory support. Hastening the maturation of fetal lungs would prevent a significant portion of the deaths among these infants.

By the early 1970's, extensive studies with animal models had demonstrated the effectiveness of antenatal administration of dexamethasone, which is a synthetic corticosteroid, in accelerating lung maturation and diminishing the incidence of NRDS. Only one large, controlled, double-blind study had been conducted, the preliminary results of which showed a reduction in the incidence of NRDS following administration of betamethasone to mothers 24 hours after the onset of premature labor. No data had been published on the short-term effects of the steroid on the neonate and the mother and on long-term effects of the dexamethasone on the infant, although newborns frequently are treated with corticosteroids for a variety of conditions.

With that background, the Collaborative Study on Antenatal Steroid Therapy was initiated in 1976 under the sponsorship of the Division of Lung Diseases, and it involved the participation of one Canadian and four U.S. medical centers. The study was designed to determine whether the administration of corticosteroids 24 to 48 hours before parturition would prevent the development of NRDS. A secondary purpose was to investigate any short-term or long-term adverse effects of the drug on the mother and to demonstrate differences in total and cause-specific infant mortality rates between newborns of the mothers who received antenatal steroids and of those whose mothers did not.

The participating clinical centers screened nearly 8,000 pregnant women at risk for premature delivery to find those eligible for the study. Two groups, comprising a total of 696 women, were formed. The control group consisted of women who received placebo injections on the same schedule as the women in the treatment group. The treatment group was made up of women who received up to 20 mg of dexamethasone divided into four doses 12 hours apart. Some women (less than 25 percent) delivered before receiving three or more injections.

Immediately upon delivery and at specified intervals afterwards, the infants were administered a battery of tests to detect NRDS and to provide answers to questions about short-term effects of the drug on the fetus. The latter part of the study is still under way and will be concluded in 1983, when the last of the tests will be administered to infants as they reach 3 years of age. To date, no short-term adverse effects have been found in infants or mothers. Surprisingly, the beneficial effect of the drug was noted only among female infants in single deliveries. Approximately 1 of every 5 girls born prematurely to mothers not treated with dexamethasone had NRDS, whereas only 1 of every

20 female babies had NRDS if their mothers had received dexamethasone.

The potential usefulness of this application of dexamethasone is limited by certain factors. For reasons still unknown, white male premature babies were not benefited at all by their mother's being given the drug. Also, twins and other multiple births did not show any less incidence of NRDS in the treated group, and questions about the long-term effects of dexamethasone remain to be answered. Nevertheless, it is encouraging that this form of therapy has the potential (based on the births of female infants alone) to prevent at least 15,000 cases of NRDS every year and thus save approximately $200 million for neonatal intensive care.

Programs in the third categoric area of the Institute, that of blood diseases, have been directed to the prevention of some of the most debilitating diseases. Hepatitis B is an ever-present threat to workers in the health field and to other specific groups. An intensive effort has been mounted to develop the means to protect those who are at risk of contracting the virus. Other prevention programs have been designed to increase professional and public awareness of heritable blood diseases such as sickle cell anemia and thalassemia.

The idea of a vaccine against type B hepatitis was conceived as early as 1964 when researchers found immunologically similar particles in the blood of an Australian aborigine and in type B hepatitis patients. Shortly thereafter, other investigators obtained blood containing the surface antigen, diluted it, heated it to inactivate any infectious virus, and injected the resulting preparation into children who were entering a facility for the mentally retarded. In spite of the extremely high incidence of type B hepatitis in this facility, the children receiving the "vaccine" did not contract the disease.

Type B hepatitis virus is one of the agents that cause acute viral hepatitis. Type B hepatitis (formerly called serum hepatitis because it is frequently transmitted through blood transfusions) may lead to chronic hepatitis and cirrhosis, and it has been implicated worldwide as a principal cause of liver cancer. The virus is present in the blood of infected individuals, and it can also be spread through breast milk, saliva, and semen. Estimates of the number of type B hepatitis cases in the United States each year range from 80,000 to 150,000, with an additional 800,000 carriers, or people who can transmit the disease but who have no overt symptoms of it. Of those who develop the disease, 1 to 2 percent die from it.

The effectiveness of a vaccine against type B hepatitis was tested in a 2-year clinical trial in which more than 13,000 male volunteers were screened and 1,083 were selected. Homosexuals

made up the study group, which consisted of men who at the start of the study had neither type B hepatitis antigen nor antibody in their blood. This group was selected because in it, the incidence of type B hepatitis is at least 10 times greater than that of the general population.

The volunteers were divided into two groups. The first group received the hepatitis vaccine at the beginning of the study, a second injection 1 month later, and a third and final injection 6 months after entering the study. The second group, the controls, received placebo injections at the same intervals. At the end of 18 months, the researchers compared the incidence of type B hepatitis in the two groups. Of the vaccinated group, 96 percent developed antibodies to type B hepatitis virus, and 1.4 percent of this group developed hepatitis. Those who developed the disease were among the 4 percent who had not developed antibodies. In contrast, 18 percent of the placebo group developed type B hepatitis. With the use of the vaccine, a 92 percent reduction was seen in the incidence of the disease.

Inoculation against type B hepatitis is not practical or necessary for the general population. Those whose occupations or lifestyles place them in greater likelihood of contracting the disease, however, can benefit. The vaccine now is being produced commercially.

Other control programs in the blood diseases and blood resources area have concentrated on sickle cell anemia and Cooley's anemia. Despite the fact that in 1972 much was known about these diseases and their ramifications, public awareness of them remained poor, even among the population who were most at risk. In addition, the actual prevalence and distribution of Cooley's anemia were not yet determined. Institute programs were focused on informing the public about these diseases and accumulating the data needed to determine prevalence.

For some time, scientists have understood the hereditary defect in the hemoglobin molecule that is responsible for sickle cell anemia. The normal adult hemoglobin molecule comprises two alpha and two beta chains. This basic structure also holds true in the hemoglobin of the sickle cell patient, but an aberration in the beta chain results in a hemoglobin molecule that, under conditions of reduced oxygen, distorts the erythrocyte membrane and reshapes it to the characteristic crescent (sickle) shape. These rigid cells are frequently unable to circulate through the smaller blood vessels, and they can occlude such vessels. The resulting lack of oxygen in the tissues "downstream" results in recurrent debilitating pain, which has been given the name sickle cell crisis. Over time, these tissues suffer chronic damage, which leads to organ dysfunction. In addition, the abnormal red blood cells are destroyed by the body at a rate faster than they

can be replaced by the bone marrow. Other problems result from this chronic anemia and the frequent blood transfusions that patients receive.

Despite the knowledge of the genetic disorder responsible for sickle cell anemia, scientists in 1972 had not been able to devise an effective treatment for the disease or to shorten or prevent the crisis episodes. In addition, the general public and many health care practitioners had limited or inaccurate knowledge about the disease and its effects. In an attempt to change that situation for the better, the Institute embarked on an ambitious professional and public education program. The Sickle Cell Disease Program was initiated in 1972 to provide a focus and impetus for needed basic research on sickle cell anemia, coordinate an ambitious public education program, encourage and expand community programs in screening and counseling activities, and improve the clinical care of sickle cell patients.

To that end, 15 Comprehensive Sickle Cell Centers were established to concentrate resources, facilities, and personnel in a coordinated approach to solving the multiplicity of problems related to the disease. From these centers and other research programs have come promising clinical findings that permit prenatal and neonatal diagnosis of sickle cell disease and offer the clinician a tremendous advantage for clinical management. Professional programs were developed for prenatal counseling of couples whose offspring would be at risk for sickle cell anemia, to enable them to arrive at educated and well-informed decisions about family planning. In addition, a clinical protocol was developed for emergency room personnel to highlight the symptoms and outline various diagnostic and treatment regimens for sickle cell crises. The public education efforts included dissemination of information through high school biology teachers to increase their awareness as well as that of their students of the seriousness of the disease.

Recent prevention-related efforts include the continuation of public and professional education programs and the establishment of September 1982 as "Sickle Cell Disease Month." Research has begun on a machine for extracorporeal carbamylation of whole blood for treatment of sickle cell disease. Clinical research includes programs to reactivate the production of fetal hemoglobin, the structure of which includes a gamma chain of hemoglobin in place of the beta chain in the adult hemoglobin molecule. Success has recently been achieved in this program, but long-term clinical trials are yet to be initiated.

Other NHLBI prevention efforts include intervention programs among the population at large to change lifestyle habits to reduce risk factors, and, potentially, to reduce morbidity and mortality from cardiovascular diseases. A number of intervention programs,

some involving numerous communities, are under way with Institute funding.

Community intervention programs are under way in three states--California, Minnesota, and Rhode Island--in an attempt to demonstrate the effectiveness of community intervention among a broad-based population rather than among persons at high risk for developing heart disease. The purpose of the studies is to demonstrate whether utilization of widespread community-based resources, including schools, health professions, local governments, and local media, can be effective in lowering risk factors among the population; and also whether this change will be reflected in reduced coronary artery disease morbidity and mortality if residents of the communities do indeed respond to the campaign to lower risk factors.

A secondary and equally important purpose of these programs may also be realized. The studies will help to demonstrate the potential effectiveness of an integrated program involving the media, civic organizations, industry, schools, and public health professionals in achieving the primary goal of the program.

Another study is the Cardiovascular Risk Reduction Study, which is under the direction of the Medical College of Virginia. It is designed to measure the effects of educational intervention for patients at high risk of cardiovascular and cerebrovascular diseases. The study is divided into four components. The first seeks to detect carotid artery disease among patients who are asymptomatic but who are found to have occlusion of the carotid arteries, and to offer these patients a behavioral education program concerning transient ischemic attacks. The remaining three components are behavioral education programs for high-risk patients and their families. One is for patients who have hypertension, and it focuses on reduction of salt intake; another concentrates on prudent diet information for persons with coronary artery disease; and the last is an attempt to induce smoking cessation among individuals who have coronary artery disease. These studies are centered in five demographically diverse communities in Virginia.

The prevention of cardiovascular disease remains a major priority of the National Heart, Lung, and Blood Institute, and the Office of Prevention, Education and Control remains the principal channel through which the Institute's efforts are transferred to the public health and lay constituencies.

Through collaborative efforts with other government agencies and the private sector--business and industry, and voluntary, professional, and other organizations--the OPEC has helped to multiply its resources and extend the reach of prevention efforts to wider audiences. The types of collaboration range from

replicating NHLBI booklets for thousands of employees to the development of sophisticated risk-reduction programs.

The U.S. Army, for example, reprinted 9 million copies of the Eaters' Almanac, a series of 26 nutrition education booklets, for circulation to Army personnel and their families worldwide. P&C Food Stores distributed 1.5 million copies of the series through its supermarkets in the Northeast. AT&T Longlines in Virginia, the Connecticut and Maryland Departments of Health, the Sentinel Star Newspaper in Orlando, Florida, and the U.S. Navy have invested staff time, facilities, and funds to reprint and distribute the NHLBI consumer booklet Exercise and Your Heart to their employees and to the communities they serve. Pfizer Laboratories; Searle Pharmaceuticals; Merck, Sharp, and Dohme; and Upjohn Pharmaceuticals reprinted thousands of high blood pressure pamphlets, posters, and other materials for NHLBI distribution to community programs throughout the country. The National Life Insurance Company reprinted 1 million pamphlets of High Blood Pressure, Facts and Fiction to send to clients, many of whom are black. Collaborators have included organizations from abroad; the Universidad Nacional de La Plata translated into Spanish and reprinted a series of NHLBI therapeutic diet booklets for hospital patients in Argentina.

In other collaborative efforts, the NHLBI, through the OPEC, has acted as a catalyst in establishing substantial risk reduction programs. Working with groups such as General Motors, Bethlehem Steel, Boeing Aircraft, and the United Steel Workers of America, the OPEC has provided advice and technical assistance in establishing worksite prevention programs, particularly for high blood pressure control. Seminars on cardiovascular health at the worksite have been developed and presented for the American Occupational Medical Association and the American Association for Occupational Health Nurses to assist these groups to initiate projects within their own companies.

Insurance companies, which are organizations with programs that are ubiquitous throughout industry, have a vested interest in health promotion activities at the worksite. The OPEC, therefore, has entered into a number of cooperative efforts with several insurance companies (Travelers, Metropolitan, and Blue Cross-Blue Shield) to assist in developing, expanding, and evaluating disease prevention and health promotion programs at the worksite, both within the companies and among group subscribers. In addition, the Institute is working as a catalyst to promote the policy among insurance companies of offering reduced premiums to hypertensives who maintain their blood pressure under control. It is possible that the successful initiation of such a policy among the companies will be an added incentive for hypertensive patients to adhere to their treatment programs.

These cooperative programs with the private sector, the insurance industry, and public media reflect the acute awareness of the Institute of the benefits to be gained in disease prevention and health promotion through such programs. Channeling research knowledge through networks of voluntary organizations, industrial unions, business consortia, and professional associations multiplies the resources available to disseminate knowledge and improve the public health without the need for large investments of taxpayer dollars.

The effectiveness of these prevention programs can readily be seen. Cardiovascular mortality began a precipitous decline in 1972, when the National High Blood Pressure Education Program was initiated. From 1972 to 1981, stroke deaths alone declined nearly 45 percent, or approximately 5 percent a year. At a time when mortality from certain other causes is increasing, it is gratifying to observe the decline in mortality statistics from cardiovascular disease. Obviously, the NHBPEP is not responsible for the total decline in the mortality figures, but it seems to have been a catalytic presence that contributed significantly to the overall benefit.

It should also be noted that prevention programs do not exist in a vacuum. Major clinical trials are based on findings in basic and clinical research that are then applied to a larger population. The results of the clinical trials must be offered to the medical profession as quickly as possible to educate the primary care physician as to the new findings. Finally, the results must be disseminated through as many channels as possible to the general public to maintain their awareness of the value of prevention and offer them timely health information that they can use. The prevention program is only one link in a strong chain that joins the laboratory researcher to the practicing physician and the lay public.

Recent Prevention Legislation

The 91st Congress

The 91st Congress (1969-1971) enacted a law to facilitate the prevention of heart, blood vessel, lung, and blood diseases. Known as the Public Health Cigarette Smoking Act of 1969,[1] the law, which extended government protection of the public health,

[1] P.L. 91-222.

banned cigarette advertising on radio and television and changed the language of the warning label on cigarette packages from "The Surgeon General Has Determined That Cigarette Smoking May Be Hazardous to Your Health" to "... is Dangerous to Your Health." (Emphasis added.) The hearing[2] that led to the act was necessitated by the expiration of the Federal Cigarette Labeling and Advertising Act,[3] and it addressed the finding of the Federal Trade Commission[4] "that warnings on packages of cigarettes, no matter how strongly worded, would be substantially negated and nullified by the content and persuasiveness of current cigarette advertising." The industry had spent $311.9 million in 1967 on cigarette advertisements, "which, in the main, portrayed cigarette smoking as a desirable physical and social activity consistent with good health." In support of its finding, the commission displayed data showing a steady increase in the number of cigarettes sold per year from 1964 through 1968.

The 92nd Congress

Two laws enacted by the 92nd Congress (1971-1972) addressed prevention of diseases within the NHLBI purview. The first[5] was concerned with a program for the prevention of sickle cell anemia, and it amended the Public Health Service Act by establishing a Federal program for diagnosis, prevention, and treatment of the disease. The program also included voluntary screening, counseling, and education of carriers of the sickle cell trait. Committee reports[6] leading to the law reviewed the body of knowledge about the disease and the readiness of the research community to develop improved therapies. The law is cited as the National Sickle Cell Anemia Control Act.

The second law was much broader in scope. Known as the National Heart, Blood Vessel, Lung, and Blood Act of 1972,[7] it enlarged the authority of the National Heart and Lung Institute

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[2] Hearing before the Consumer Subcommittee of the Committee on Commerce, United States Senate, Ninety-First Congress, First Session, on H.R. 6543.

[3] P.L. 89-92, July 27, 1965.

[4] Report to Congress Pursuant to the Federal Cigarette Labeling and Advertising Act, June 30, 1969.

[5] P.L. 92-294.

[6] 92d Congress, 2d Session, House of Representatives, Report No. 92-923; and 92d Congress, 1st Session, Senate Report No. 92-557.

[7] P.L. 92-423.

"to advance the national attack upon heart, blood vessel, lung, and blood diseases." The act mandated the Director of the Institute to develop a national program providing inter alia for "investigations into the epidemiology, etiology, and prevention of all forms and aspects of heart, blood vessel, lung, and blood diseases, including investigations into the social, environmental, behavioral, nutritional, biological, and genetic determinants and influences involved in the epidemiology, etiology, and prevention of such diseases." As reported out of the House of Representatives Committee on Interstate and Foreign Commerce, the bill placed special emphasis "on informing the public of the effect of reduction of known risk factors in preventing these disorders."[8] The legislation also required the Secretary of Health, Education, and Welfare to establish an Interagency Technical Committee. The purpose of this committee was to coordinate Federal health programs and activities related to heart, blood vessel, lung and blood diseases, and blood resources to ensure that the programs were technically sound and to encourage the agencies to exchange information about their programs. The Director of the NHLBI serves as chairman of the IATC.

The 93rd Congress

The 93rd Congress (1973-1974) addressed four NHLBI areas of research and enacted legislation in none of them. A bill[9] to increase appropriations for the National Heart and Lung Institute by raising the excise tax on cigarettes died before reaching committee. It would have amended the Internal Revenue Code of 1954. Early in this Congress, a movement reflected in 16 House bills and 1 Senate bill was organized to establish a Federal blood bank program.[10] The act would have encouraged voluntary donations of pure and safe blood, required licensing and inspection of blood banks, and established a national registry of blood donors. The House bills did not progress beyond introduction. The Senate version was referred to committee, which requested comments from the Justice Department, the General Accounting Office (GAO), the Office of Management and Budget, and the Department of Health, Education, and Welfare. Only the GAO responded, and the bill died in committee. Concern for serum hepatitis and sickle cell anemia provided the basis for two other bills. One[11] would have provided

[8] 92d Congress, 2d Session, Report No. 29-1108, p. 3.

[9] H.R. 17179.

[10] H.R. 160, H.R. 264, H.R. 804, H.R. 1524, H.R. 3502, H.R. 4710, H.R. 8386, H.R. 8984, H.R. 8985, H.R. 8986, H.R. 9224, H.R. 9254, H.R. 9808, H.R. 9911, H.R. 9912, and S. 1402.

[11] H.R. 837.

funds for research to detect serum hepatitis prior to transfusion and transmission of the disease, and the other[12] would have established a National Sickle Cell Anemia Institute. Neither bill reached committee.

The 94th Congress

Legislation enacted by the 94th Congress (1975-1976) in the Health Research and Health Services Amendments of 1976[13] was far-reaching. A stated purpose of the amendment was "to enlarge the authority of the National Heart, Lung, and Blood Institute in order to advance the national attack upon heart, blood vessel, lung, and blood diseases and to enlarge its authority with respect to blood resources." Adding the word "blood" to the name of the Institute, the amendments mandated an assistant director for prevention, education, and control and authorized "ten new centers for basic and clinical research into, training in, and demonstration of, advanced diagnostic, prevention, and treatment methods... for blood, blood vessel diseases, research in the use of blood products, and research in the management of blood resources." In addition, genetic diseases, including the voluntary diagnosis and control of them, were singled out for specific legislation. Another provision mandated the establishment of "a national program to provide for basic and applied research, research training, testing, counseling, and information and education programs with respect to genetic diseases, including sickle cell anemia, Cooley's anemia, Tay-Sachs disease, cystic fibrosis, dysautonomia, hemophilia, retinitis pigmentosa, Huntington's chorea, and muscular dystrophy."

Although having no direct bearing on the NHLBI, a series of amendments[14] in 1976 to the Public Health Service Act illustrates the attitude of this Congress with regard to disease prevention. At the departmental level, the Secretary was required to formulate national goals, and a strategy to achieve them, with respect to health information and health promotion, preventive health services, and education in the appropriate use of health care. The amendments authorized research programs, community programs, information programs, and disease control programs, and required the Secretary to submit annual status reports to the President for transmittal to Congress on activities authorized by the legislation.

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[12] H.R. 3687.

[13] P.L. 94-278.

[14] P.L. 94-317.

This Congress also created the National Diabetes Advisory Board.[15] Made up of a number of ex officio members, including the Director of the NHLBI, the board has the mandate to review and evaluate the implementation of the long-range plan to combat diabetes mellitus formulated by the National Commission on Diabetes under the National Diabetes Mellitus Research and Education Act and to give advice and make recommendations with respect to guidelines, policies, and procedures of Federal diabetes programs.

In this Congress, a number of bills on prevention carried over from the 93rd Congress failed enactment. Renewed efforts were made to increase NHLBI appropriations by raising the excise tax on cigarettes,[16] to create a National Sickle Cell Anemia Institute,[17] and to authorize a national blood bank program[18] and a serum hepatitis program.[19] In two new areas, bills were introduced that would have provided programs to diagnose and treat hemophilia[20] and would have added a list of specific diseases to the warning label on cigarette packages.[21]

The 95th Congress

In the Clean Air Act Amendments of 1977,[22] the 95th Congress (1977-1978) created a Task Force on Environmental Cancer and Heart and Lung Disease. Including representatives from the NHLBI, the task force has a broad responsibility. It recommends a comprehensive research program to determine the relationship between environmental pollution and human cancer and heart and lung disease, strategies to reduce or eliminate the risks of cancer and other diseases associated with environmental pollution, and measures to prevent or reduce the incidence of environmentally related cancer and heart and lung diseases. Also, it coordinates research by and stimulates cooperation between Federal agencies having authority in these areas. The task force must report annually to Congress on the problems and progress of its work.

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[15] P.L. 94-562.

[16] H.R. 1605, H.R. 3632, H.R. 4135, H.R. 8744, H.R. 2619, and S. 2896.

[17] H.R. 4095.

[18] H.R. 3699.

[19] H.R. 684.

[20] H.R. 686 and S. 755.

[21] H.R. 596.

[22] P.L. 95-95.

In amendments to the Public Health Service Act, this Congress also authorized a National Center for Health Care Technology (NCHCT), with a Council consisting of numerous ex officio members, including the Director of the NIH.[23] Members of the Council are obligated to report annually to the Council and to the NCHCT a listing of all health care technologies. The term is defined by the law as "any discrete and identifiable regimen or modality used to diagnose and treat illness, prevent disease, maintain well-being, or facilitate the provision of health care services." An amendment[24] directly affecting the NHLBI authorized "programs of continuing education for health and allied health professionals in the diagnosis, prevention, and treatment of such [heart, blood vessel, lung, and blood] diseases and information programs for the public respecting the prevention and early diagnosis and treatment of such diseases."

Some of the amendments[25] of the 95th Congress to the Public Health Service Act were focused on the Department itself. The Secretary was authorized to "make grants to State health authorities to assist them in meeting the costs of establishing and maintaining preventive health service programs for screening for, the detection, diagnosis, prevention, and referral for treatment of, and follow-up on compliance with treatment prescribed for, hypertension"; and the Secretary was given a mandate to make grants to states to assist them in planning and developing preventive health service programs "designed to reduce, through primary or secondary prevention of risk factors and causative conditions, the mortality rate for one or more of the five leading causes of death in a State." This Congress also mandated that the Secretary establish in the Secretary's office a Select Panel for the Promotion of Child Health. The panel was charged with formulating specific goals with respect to the promotion of the health status of children and expectant mothers and with developing a comprehensive national plan for achieving them. In addition, the Secretary, acting through the National Center for Health Statistics, was required to submit to the Congress triennial profiles of national disease prevention data.

The 96th Congress

In the Health Programs Extension Act of 1980,[26] the 96th Congress (1979-1980) created three interagency coordinating

[23] P.L. 95-623.

[24] P.L. 95-622.

[25] P.L. 95-636.

[26] P.L. 96-538.

committees--one for arthritis, one for diabetes mellitus, and one for digestive diseases--and a national advisory board for each of these disease categories. The NHLBI director was made an ex officio member of the National Diabetes Advisory Board. The basic purpose of this legislation was to develop research plans coordinated among the various NIH institutes for addressing the diagnosis, treatment, and prevention of these diseases, and each of the advisory boards was mandated periodically to update the plan within its purview to ensure its continuing reliability. Two bills that would have affected the NHLBI failed in this Congress. One would have, again, established a National Sickle Cell Anemia Institute,[27] and the other[28] would have established a national policy on health promotion and disease prevention. The policy would have focused on the funding of programs aimed at primary prevention of disease.

The 97th Congress

The 97th Congress (1981-1982) is considering several bills that could have an impact on the NHLBI; two appear to be significant at the present time. One[29] would establish a health promotion and disease prevention program, which is similar to that contained in the bill introduced in the previous Congress. The other[30] would appropriate funds specifically for preventive health service programs, including hypertension and tuberculosis.

[27] H.R. 1451.

[28] H.R. 3202.

[29] H.R. 2212.

[30] H.R. 3688.

3. International Programs

Contents

3. International Programs

The health problems addressed by the National Heart, Lung, and Blood Institute programs are not unique to the people of the United States. They are international in scope and magnitude, and they affect hundreds of millions of people throughout the world. Physicians, scientists, and technologists the world over are devoting their efforts to controlling heart, blood vessel, lung, and blood diseases and to improving the quality of blood resources required by modern medicine. Countless opportunities now exist for U.S. researchers to join forces with organizations and individuals in other countries to improve the health of people everywhere.

In 1972, the NHLBI had only a modest international involvement through a limited number of individual grants and contracts awarded to foreign scientists in areas relevant to the Institute's National Program. Now, in 1982, the Institute is engaged in formal and informal activities with other countries and with international organizations such as the World Health Organization (WHO) and the Pan American Health Organization (PAHO). In recognition of the Institute's contributions to international health, the WHO in 1980 designated the NHLBI a Collaborating Center for Cardiovascular Research and Training in the Americas.

Perhaps the strongest evidence of growth in international activities is seen in the Institute's increased participation in joint research under bilateral government agreements. At the start of the past decade, there were no such agreements for cooperation in research. As the decade closed, the Institute was actively participating in 14 bilateral agreements with 12 governments involving hundreds of scientists from the United States and other countries. Most of the agreements focus on the epidemiology, prevention, and control of cardiovascular disease, which is the leading cause of death in many of the cooperating nations.

Also during the last decade, the NHLBI awarded 178 grants and contracts to scientists in 21 countries and supported 90 U.S. fellows for postdoctoral training in foreign countries. In the same period, the Institute's Division of Intramural Research received 531 scientists from 38 countries for joint research.

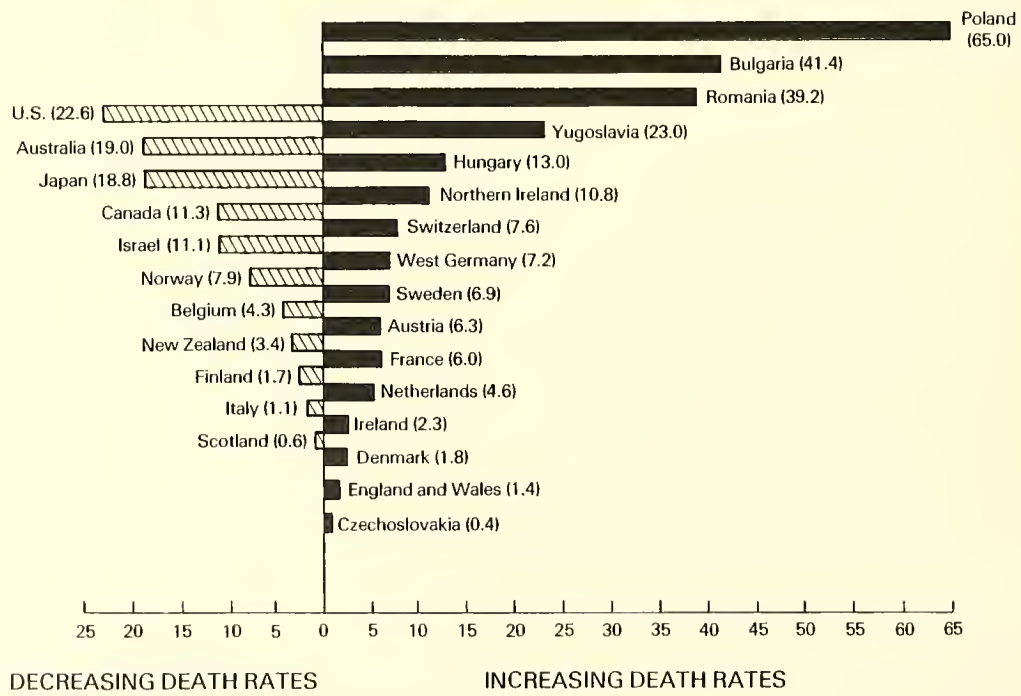
This increase in international activity resulted from specific presidential and congressional initiatives to strengthen

the U.S. role in international health. There were other factors affecting the increase:

- The national program mandated by the National Heart, Blood Vessel, Lung, and Blood Act of 1972 significantly expanded the scope and depth of the Institute's program and thereby expanded the Institute's ability to engage in international collaboration.

- The Department of State and the Department of Health, Education, and Welfare (now Health and Human Services) took important steps to increase the U.S. role in international cooperation in medicine and health. At the initiative of these departments, the U.S. Government has entered into bilateral agreements for cooperation in science, technology, and health.

- Other nations showed an increased interest in cooperating with the NHLBI. The success of the National Program in bringing about a decline in cardiovascular disease was an important factor. As figure 1 shows, the United States



*Percent change is based on data from 1969 and 1977.

Figure 1. Percent Change in Death Rates for Coronary Heart Disease Among Men Ages 35 to 74 in Selected Countries*

now leads the world in decline in death rates from coronary heart disease, although the U.S. rate is still among the highest in the world (figure 2).

In addition, major shifts in international relations occurred during the 1970's, which opened up new vistas for international collaboration in health. For the first time in many decades, it became possible for U.S. scientists to cooperate with scientists from the Soviet Union and from the People's Republic of China in planning, implementing, evaluating, and reporting joint research. These new cooperative relationships have added more than a billion people to the population groups available for joint epidemiological studies. Also during the 1970's, important new research linkages were initiated between the United States and developing countries in Africa, Asia, and South America. Many investigators and administrators from these continents visited the NHLBI to discuss possible areas of cooperation. As a result of these developments, the scope of the Institute's international activities in 1982 is vastly different from that in 1972.

These international activities have also facilitated the transfer of developments in other countries to medical practice in the United States. Many of the medical advances now enjoyed by Americans had their origin in laboratories and clinics outside this country. Specific examples include:

HEART AND VASCULAR DISEASES

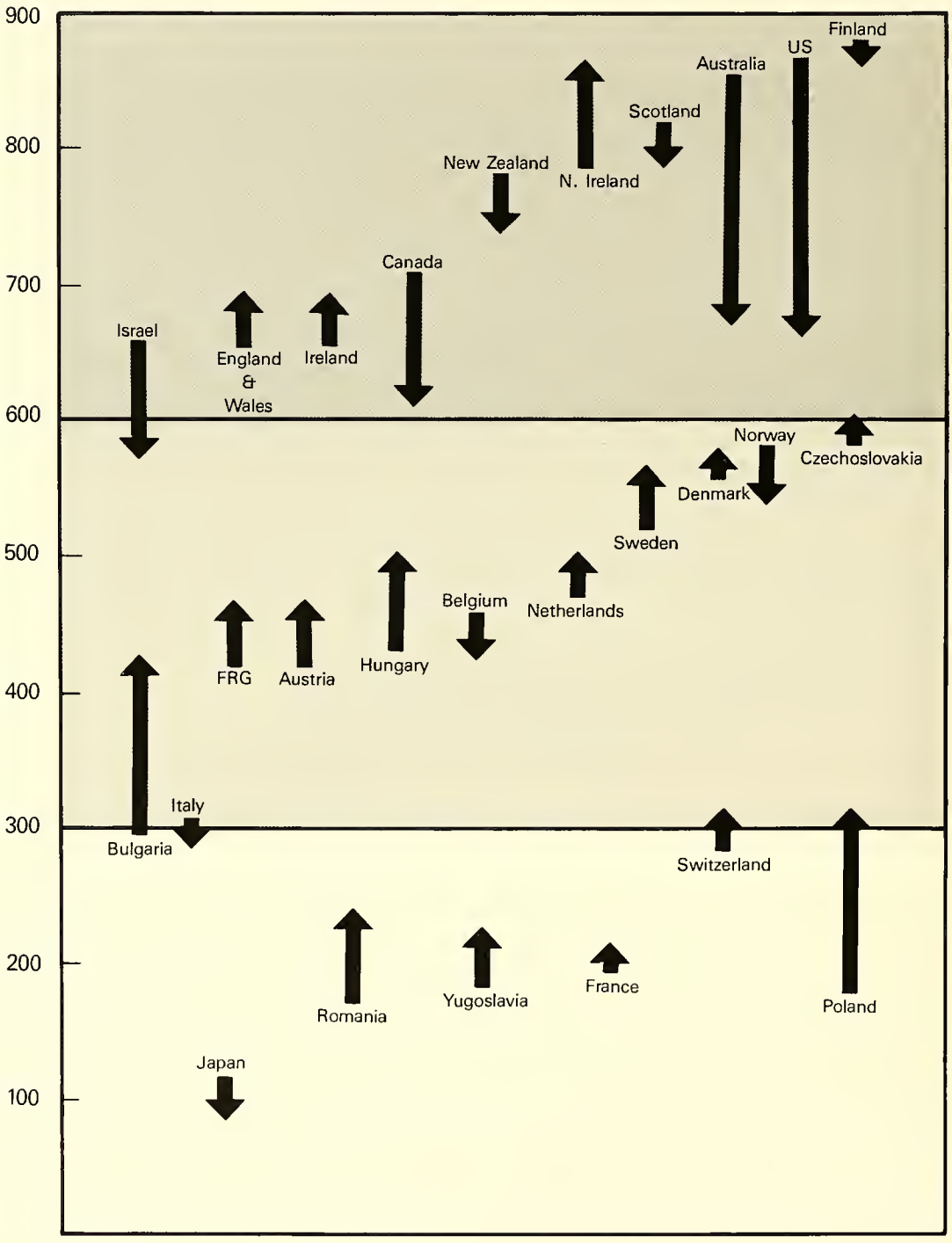
- Swiss scientists pioneered the work on coronary angioplasty, which may obviate bypass surgery in many patients.

- British scientists contributed the use of beta-blocking drugs in coronary heart disease.

- An Italian physician performed new work on the role of spasm of coronary blood vessels in ischemic heart disease.

- British scientists developed computerized tomography, and one of them recently received a Nobel prize (shared with a U.S. scientist) for this discovery. This technique has greatly enhanced the possibility of detecting abnormalities in the cerebrovascular system.

- Researchers in the Federal Republic of Germany developed intracoronary injections of streptokinase. Application of this technique in the treatment of acute heart attacks is now being studied in this country.



*Rate per 100,000 Population

Figure 2. Trends in Death Rates for Coronary Heart Disease Among Men Ages 35 to 74 in Selected Countries, 1969 to 1977*

- Cardiac biopsy, which is used in the diagnosis of cardiomyopathies, was originally developed in Japan.

- A South African surgeon pioneered work on heart transplantation.

- The role of interactions between genetic and environmental factors in hypertension was pioneered in Japan.

- Japanese scientists, in cooperation with U.S. scientists, developed important new information on the protective role of protein in preventing stroke in genetically stroke-prone animals.

- U.S.-U.S.S.R. findings of strikingly higher high density lipoprotein (HDL) cholesterol levels in Soviet men in 1976 contributed to a growing interest in HDL and its inverse relation to coronary heart disease.

LUNG DISEASES

- Britain was one of the leading countries in studies of hypersensitivity pneumonitis, a widespread chronic lung disease.

- Studies in Turkey of certain zeolite deposits, similar to asbestos, that resulted in lung disease alerted U.S. scientists to the presence of similar deposits in the Salt Lake City region and to the possibility of similar lung disease problems in this country.

- Exchanges between scientists in the United States and France have helped accelerate research on the mechanisms of inflammation and on the immune mechanisms in the lung.

- Long-term epidemiological studies of lung disease in Britain and Sweden have greatly benefited U.S. researchers. For many years, Britain has collected data on the role of infection in chronic bronchitis, and Sweden has collected data on chronic lung disease. Swedish researchers first described alpha-1-antitrypsin deficiency and recently pioneered studies on the role of smoking in precipitating emphysema and very early death in individuals homozygous for alpha-1-antitrypsin deficiency.

- Scientists in Canada are providing important information on the natural history of lung disease by using advanced methods to study the relationships of structure and function in chronic obstructive lung disease.

BLOOD DISEASES AND BLOOD RESOURCES

- Swedish scientists have performed important basic structural work on coagulation proteins.
- Research in Africa, Asia, and the Soviet Union has helped lead to knowledge of the nature of abnormal hemoglobins.
- Hemoglobin conformational changes in sickle cell disease were discovered in England.
- A Polish clinical trial is examining the effect of prostacyclin in the treatment of thrombosis.
- Swedish scientists have been extracting interferon from leukocytes. A Swedish laboratory provides 99 percent of the U.S. supplies for research in this area.
- The Green Cross Corporation in Japan has produced new blood substitutes that are being tested for use in the United States. Fluosol-DA, for example, is currently being used in the United States for research purposes.
- Scientists in Scotland have developed new approaches to the treatment of hemophilia.
- Significant advances in platelet research by French scientists have led to a better understanding of the structure and function of platelets in disease.
- In Peru, research is under way on high altitude disease as a model of how individuals operate under conditions of insufficient oxygen.

Activities With Other Nations

Through international cooperation, U.S. scientists are able to conduct comparative studies with other populations, and through such mechanisms as bilateral government agreements, to reduce costs and duplications of efforts. By jointly developing protocols and by standardizing and monitoring the collection and analysis of data, several countries, for instance, can participate in the same study. The cooperation reduces the cost to each country and makes it possible to undertake studies too expensive or too wide-ranging for any one country to sponsor alone.

Important formal international activities of the NHLBI during the period 1972 to 1982 are described below.

Canada

Researchers from the United States and Canada have been cooperating for many years in several areas related to the Institute's mission, particularly in the area of clinical trials.

Beta-Blocker Heart Attack Trial

The Montreal Heart Institute was one of 31 institutions cooperating in the NHLBI-sponsored trial that was initiated in 1977. The objective of the trial was to establish whether regular administration of the beta-adrenergic blocking agent propranolol would significantly reduce mortality over a 3-year period in patients with a recent documented heart attack. The trial, which was terminated in October 1981, showed that the cumulative mortality of the propranolol-treated group was significantly lower than that of the control group.

Coronary Artery Surgery Study

The Coronary Artery Surgery Study, which was a 7-year trial, was initiated by the NHLBI in 1973 to determine the most appropriate types of therapy for patients with advanced coronary artery disease. The Montreal Heart Institute is one of 15 centers cooperating in this study, which compares the efficacy of coronary artery bypass surgery with nonsurgical therapy.

Multiple Risk Factor Intervention Trial

The goal of the Multiple Risk Factor Intervention Trial, which began in 1972, is to study prevention of first heart attacks among men aged 35 to 57 years who are at increased risk of developing coronary heart disease because they exhibit two or more of the major risk factors: elevated serum cholesterol, elevated blood pressure, and cigarette smoking. Participants in the trial have no preexisting clinical coronary heart disease. The central ECG Laboratory for this 20-center trial is located at Dalhousie University, Halifax, Nova Scotia.

Lipid Research Clinics Program

The Lipid Research Clinics Program, which was initiated by the NHLBI in 1971 jointly with 15 Lipid Research Clinics (LRC's), contributes to the improved diagnosis and management of hyperlipoproteinemia and to the understanding of its role in cardiovascular disease. The Canadian Toronto-McMaster LRC and its 14 counterparts in the United States, Israel, and the Soviet Union are

participating in population studies of the prevalence of blood lipid abnormalities, the metabolism of plasma lipids and lipoproteins, and their relationship to premature atherosclerosis. In addition, the LRC Coronary Primary Prevention Trial involves testing the hypothesis that long-term reduction of serum cholesterol in middle-aged men with elevated cholesterol will prevent or delay premature coronary heart disease.

Intermittent Positive Pressure Breathing

The clinical study Intermittent Positive Pressure Breathing is a 5-year collaborative trial begun by the NHLBI in 1977. It is evaluating the effectiveness of the long-term use of intermittent positive pressure breathing as an adjunct treatment in ambulatory patients with chronic obstructive lung disease. The University of Manitoba is one of six centers cooperating in this trial.

Continuous Nocturnal Oxygen Therapy

The Nocturnal Oxygen Therapy Trial in hypoxemic chronic lung disease was initiated by the NHLBI in 1976 and completed in 1980. The University of Manitoba was also involved in this study. Overall mortality in the nocturnal oxygen therapy group was 1.94 times that of the group given continuous oxygen therapy. Continuous oxygen therapy had a markedly beneficial effect in patients with severe pulmonary dysfunction and also appeared to benefit patients with lesser pulmonary dysfunction.

Prevention of Neonatal Respiratory Distress Syndrome

Neonatal respiratory distress syndrome causes some 8,000 to 10,000 neonatal deaths each year in the United States. The NHLBI began its Collaborative Study on Antenatal Steroid Therapy in 1976 after animal and human studies suggested that the administration of steroids to the mother late in pregnancy might protect against NRDS in premature infants. Six centers, including one at the University of Manitoba, participated in this trial. The trial demonstrated that pretreatment of mothers with dexamethasone shortly before they gave birth reduced the incidence of NRDS among their premature singleton female infants by 400 percent. Steroid treatment appeared to produce no short-term ill effects on the fetus, the newborn, or the mother. To test for potential long-term ill effects, a 3-year followup of all dexamethasone-treated mothers and their infants is under way.

Union of Soviet Socialist Republics

The U.S. Secretary of State and the U.S.S.R. Minister of Health signed a formal bilateral health agreement in 1972. The agreement calls for collaboration in seven areas: pathogenesis of arteriosclerosis; ischemic heart disease; myocardial metabolism; congenital heart disease; sudden cardiac death; blood transfusion; and hypertension. Cooperation in an eighth area, the Artificial Heart Research and Development Program, was initiated by an agreement signed in 1974. Both agreements were renewed in 1982 for another 5 years.

The eight U.S.-U.S.S.R. cardiovascular programs described below provide a forum for cooperation on problems transcending national boundaries. Twenty-one joint symposia have been held, and the proceedings have been published (or are in press) both in English and in Russian. Nearly 500 scientific papers have been published under the aegis of the exchange.

Atherosclerosis

Atherosclerosis is directly or indirectly responsible for more deaths in the United States and the Soviet Union than any other disease. Of the numerous recognized risk factors for the development of atherosclerosis, elevated blood lipids (specifically, serum cholesterol levels) have been implicated extensively and unequivocally. Low density lipoproteins (LDL) are the major carriers of cholesterol and are directly associated with an increased risk of coronary heart disease. High density lipoproteins also carry cholesterol, but they are an independent negative risk factor for premature atherosclerosis.

Under the U.S.-U.S.S.R. agreement, the Lipid Research Clinics Program was extended to include the Soviet Union in 1972. Two cooperating clinics were established and funded by the Soviet Union in Moscow and Leningrad. In addition to geographic diversity, the populations selected in both countries for the cooperative studies cover a wide range of ethnic, occupational, and age groups. Thus, a variety of cross-cultural comparisons are possible. Nine of the U.S. LRC's are collaborating with the Soviet clinics in collecting and analyzing extensive information for the first phase of prevalence studies of men aged 40 to 59 years. This number includes nearly 8,000 men from each country who were screened at a first clinic visit and over 1,000 from each country screened at a second, more comprehensive examination. A 5-year followup study to determine the mortality of a selected group of these individuals is now in progress. Also under way in the Soviet Union is a second round of prevalence studies of men and women aged 20 to 69 for subsequent comparison with their U.S. counterparts. The data have been collected according to common

protocols, which use highly standardized laboratory and screening techniques.

A joint symposium was held in Leningrad in May 1981 to present some of the results of the first 8 years of collaboration. Analyses of these joint studies provide important contrasts in population distributions of lipids and lipoproteins in middle-aged U.S. and Soviet men. One of the most striking initial observations was that middle-aged men in the Soviet Union had significantly higher HDL cholesterol levels than middle-aged men in the United States. In both countries, statistical analyses showed that avoidance of obesity and moderate alcohol intake were positively correlated with HDL cholesterol. In the U.S. sample, cigarette smoking was inversely correlated with HDL cholesterol, but there was no significant correlation in the Soviet sample for this variable.

Joint papers have been published in Soviet and American journals. The papers include descriptions of the design of the collaborative study, preliminary results in lipid and lipoprotein patterns, nutritional assessment methodology, and characterizations of joint laboratory research.

Future plans in this area include continuation of the epidemiological studies and particularly the followup study of middle-aged men; completion of the prevalence studies of men and women aged 20 to 69; analysis and publication of the results of these studies; and a second joint symposium on the new collaborative data. Three basic research areas are being considered for further collaborative work: cellular and lipid interactions at the arterial wall, structure and function studies of lipoproteins, and platelet-lipoprotein interactions.

Ischemic Heart Disease

Ischemic heart disease was identified in 1972 as the second area for joint U.S.-U.S.S.R. investigation. American and Soviet scientists began by initiating a clinical investigation that systematically compared groups of cardiac patients and the effectiveness of different treatment modalities in the two countries. Four study populations, each composed of men from 30 to 60 years of age, were established. One group consists of American patients who are treated by coronary artery bypass surgery. The second group consists of patients in the Soviet Union with comparable heart disease who are treated by a specialized pharmacological regimen. There are two reference groups, one in each of the two countries. Patients in the reference groups, chosen on the basis of their symptoms, coronary angiograms, and other characteristics, are treated by conventional therapy. If results show that the reference groups in both countries have similar characteristics on

admission and similar outcome on long-term followup, there will be a basis for comparing the long-term effects of surgery in the United States and differential intensive medical care in the Soviet Union. All patients will be followed through June 1983.

Plans have been made to continue to collaborate on studies of ischemic heart disease, exchange scientists working in this area, and share information about new therapeutic and diagnostic approaches.

Myocardial Metabolism

U.S.-U.S.S.R. cooperation in the area of myocardial metabolism is focused on joint research and on information exchange, and it incorporates several projects designed to provide new insights into the manner in which heart muscle cells obtain energy, coordinate their contractions, and respond to alterations in their environment. These studies are expected to contribute to the development of therapies that will enable a greater proportion of heart muscle to survive the oxygen deficiency associated with an acute heart attack and to the development of new and improved methods of preventing cardiac disease.

Over the past 10 years, participating U.S. and Soviet scientists with complementary skills and interests have defined numerous projects for joint investigations, and in alternating years, the scientists have visited the laboratories of each other from 1 to 3 months to conduct experiments. These efforts have included:

- A study to measure the potential beneficial effects of the drug hyaluronidase on heart attack victims.

- Studies to develop improved methods for in vivo imaging of and drug targeting to damaged heart muscle tissue following a heart attack.

- Experiments to clarify the interrelationship of the biomedical and electrophysiological events that occur during muscle contraction, including: studies of the energetics of heart muscle contraction and relaxation, particularly the role of cyclic nucleotides in these processes; investigations of calcium transport by the cardiac sarcoplasmic reticulum; and experiments to define the immunological properties of calcium ATPase of the cardiac and skeletal muscles.

- Physical studies of the cellular protein calmodulin, a calcium regulator, and how it interacts with the enzyme phosphodiesterase.

- Development of new methods to evaluate the hormone receptor apparatus in cells and to gain a better understanding of the components of the arterial wall.

Five joint symposia have been held on topics such as energy metabolism of heart muscle, cardiac ultrastructure and contraction, the action of hormones on cardiac muscle metabolism, and the pathophysiology of cardiac muscle ischemia. Proceedings are published in English and Russian.

For the future, joint work is planned in basic science areas to increase the knowledge and understanding of the fundamental metabolic processes controlling heart function.

Congenital Heart Disease

The NHLBI cooperates with the Bakulev Institute for Cardiovascular Surgery, Moscow, in joint activities to improve the surgical treatment of complex heart defects and to explore new methods of diagnosis, surgery, and postoperative care to reduce mortality from congenital heart disease. Cooperative efforts have consisted primarily of joint symposia and of exchanges of working groups, delegations, and individual physicians. Physicians from the United States and the Soviet Union have had the opportunity to witness surgery and to examine patients in both countries. This exchange permits direct observation of various techniques and critical comparisons of approaches and methods for surgical repair of defects of the heart and major blood vessels. One outcome of the exchange program was a joint study on aortopulmonary septal defect, which is an inborn cardiac abnormality that causes volume overload leading to heart failure at an early age unless the lesion is corrected. Results of this study were published in a leading U.S. surgical journal.

Four joint symposia on congenital heart disease have been held. The most recent was in Moscow in September 1980. U.S. and Soviet specialists discussed topics such as hypothermia, surgery for transposition of the great vessels, extracorporeal membrane oxygenation in the newborn, and the role of noninvasive radionuclide angiography in cardiac surgery. Proceedings of all symposia have been published. Another symposium is planned for 1983 in which U.S. and Soviet researchers will share recent advances in diagnosis and treatment of congenital heart disease.

Sudden Cardiac Death

In 1973, the United States and the Soviet Union began cooperative efforts to prevent sudden death from arrhythmias. Cooperative efforts have focused on the pathological anatomy and

electrophysiology that may lead to sudden death and on the pharmacology of possible prophylactic antiarrhythmic drugs. Activities have consisted mainly of joint symposia and of exchanges of information and investigators. The Soviet Union has provided data from a study of subjects at high risk in one area of Moscow and on patients who underwent ambulatory monitoring; the United States has made data available on subjects who had been screened for cardiac arrhythmias in the Multiple Risk Factor Intervention Trial.

Joint work on the Soviet-developed drug ethmozin has shown the drug to be effective against life-threatening arrhythmias. In a joint U.S.-Soviet study of patients with chronic, frequent, symptomatic arrhythmias who did not respond to other antiarrhythmic therapy, 54 percent of the patients treated with ethmozin showed significant suppression of their arrhythmias and virtually no side effects.

The United States and the Soviet Union have conducted joint studies of the effects of other antiarrhythmic drugs, including mexatil, lidocaine, aprindine, and aconitrine. Other topics of collaboration include methods for studying electrophysiological events occurring at the infarct site, the study of mechanisms of arrhythmia in the late stages of myocardial infarction, and ultrastructural changes resulting from oxygen deficiency.

Early in the exchange program, U.S. scientists learned about the Soviet use of nitrous oxide for quieting patients experiencing a heart attack. In followup studies, a U.S. scientist substantiated the effectiveness of the drug. This treatment is now used in the United States.

Data have also been exchanged on the epidemiological aspects of sudden cardiac death. Preliminary data indicate that chronological trends in the incidence of various aspects of coronary heart disease (CHD) can be identified and explained by analysis of morbidity data from study populations in both countries. These studies suggest an important role for complex arrhythmias as predictors of sudden death.

Future plans include joint research on the mechanisms and treatment of sudden cardiac death, particularly in the areas of pathological anatomy, electrophysiology, clinical aspects, epidemiology, and higher nervous activity in arrhythmias.

Transfusion of Blood and Blood Components

In 1973, the United States and the Soviet Union began cooperative efforts in an area referred to as "Transfusion of Blood, Its Components, and Prevention of Hepatitis with Particular

Reference to Cardiovascular Surgery." These efforts have focused on joint research on prevention of posttransfusion hepatitis in cardiovascular surgery; transfusion of whole blood and its components, as well as the infusion of blood substitutes during cardiovascular surgery; the treatment and management of patients with abnormal hemostatic mechanisms; and the physiological and pathological alterations of the vascular system as a result of transfusions.

In 1977, the two nations developed a protocol for a cooperative study entitled "Measurement of Hepatitis Type B Markers in Sera from Blood Donors in the U.S.A. and U.S.S.R." The purposes of the study were to compare the frequency of hepatitis viral antigens and antibodies among U.S. and Soviet blood donors and to compare, in the same sera, the results of serological tests used in the United States and the Soviet Union for hepatitis type B markers. Results of the study, which was completed in 1979, permitted the calculation of age and sex prevalence of hepatitis B and hepatitis A markers within each country and allowed comparison of the methodologies used in the Soviet Union and in the United States.

U.S. and Soviet methods for preparing antihemophilic factors have also been compared. The Soviet thaw-centrifugation procedure, designed to separate blood components from frozen plasma, was initially thought to have broad applicability since it results in high yields of protein fractions that can be used to treat hemophilia A and B, acquired coagulation defects, and other blood component deficiency diseases. Subsequent studies, however, indicate that this technique is not suitable for the mass production of these fractions by automated procedures.

In recent years, U.S. and Soviet scientists have developed an increasing interest in bleeding and clotting disorders, with particular emphasis on hemophilia and other genetic bleeding diseases. The possibility of joint studies is being explored in the areas of genetic polymorphism and clinical evaluation of hereditary blood disorders found in different geographic locations.

Plans for further collaboration include the continued exchange of scientists conducting research on blood substitutes, posttransfusion hepatitis, and apheresis. The Third U.S.-U.S.S.R. Joint Symposium on Blood Transfusion will be held in Moscow in 1983.

Hypertension

In 1977, the U.S.-U.S.S.R. Joint Committee added hypertension to areas of collaboration covered by the cardiovascular agreement.

Activities focus on the exchange of information, exchanges of scientists, joint working meetings, and joint symposia. The aim of this collaboration is to contribute to the understanding and control of hypertension through exchanges of information on the clinical, psychophysiological, behavioral, epidemiological, and preventive aspects of this "silent" killer.

As a result of exchanges during the Third Joint Symposium on Hypertension, held in May 1981, U.S. and Soviet researchers identified biobehavioral, epidemiological, and preventive aspects of hypertension as areas for mutual exploration. Specific proposed collaborative activities include: primary and secondary prevention of mild hypertension in organized population groups, communities, and patients; the role of risk factors in hypertension; the role of the nervous system; psychophysiological aspects (including tolerance to psychological stress), learning, and the environment in the etiology and development of hypertension; and psychotherapy and behavioral aspects of intervention (for example, behavior modification, relaxation, and biofeedback).

Soviet scientists reported interesting findings on the use of biobehavioral techniques in the control and prevention of hypertension. Studies have been conducted in the U.S.S.R. on the role of the environment in causing emotional stress and on the use of autogenic training to control stress and blood pressure. In one study, it was found that autogenic training in patients with essential hypertension improved the psychological status of the patients and, more important, had a pronounced hypotensive effect so that lesser drug dosages were required.

Future plans include continued exchanges of information between U.S. and Soviet working groups on population studies and on biobehavioral research. The U.S. and Soviet cochairmen are responsible for gathering information regarding current studies in their own country and for coordinating the distribution of scientific information from the other country to serve as a basis for identifying followup activities. In the area of epidemiology, the working groups have exchanged information about hypertension control programs in the work setting, correlates of blood pressure disturbances in the United States, and systolic hypertension in the elderly.

Cardiac Assist Devices

Mutual interest in the development of better technology for mechanically assisted circulation resulted in a U.S.-Soviet agreement for collaboration signed in 1974. Technical working teams of physicians, scientists, and engineers have focused on the development of better circulatory assist devices as part of the overall study of the complex physiology of assisted circulation.

This program involves exchanges of scientific and technical information, particularly information about surgical techniques for implantation of artificial devices, the design and manufacture of implantable devices, and the structure and function of circulatory control consoles. Joint activities also include conferences, workshops, and meetings of experts, exchanges of specialists and delegations, and preparation of joint publications and technical manuals. Joint symposia were held in 1979 and 1981, and their proceedings have been published. The two nations have exchanged and tested several circulatory assist devices, and both U.S. and Soviet scientists have demonstrated their surgical methods of implanting a cardiac replacement device in calves.

U.S. and Soviet biomaterials specialists developed a proposal for an exchange project in the biomaterials area. The project, which uses in vitro techniques, emphasizes the evaluation of the blood compatibility of several frequently used biomedical polymers. The proposed cooperative activity is designed to characterize the adsorption of human albumin to well-characterized materials to achieve a better understanding of the basic mechanisms of blood-material interactions and to assess the comparability of experimental results among laboratories. Followup arrangements are in progress for exchanges of materials and results of experiments.

Other planned collaborative activities include the development of joint publications, exchanges of device components, and continued exchanges of specialists working in the areas of intraaortic balloons, left ventricular assist devices, cardiac replacement devices, biomaterials, and evaluation of components of artificial circulatory support systems in vitro.

Israel

Cooperative research with Israel to study determinants of cardiovascular disease has been funded by NHLBI grants and contracts at least since 1971. Study of the unique population mix in Israel has provided many clues to the relative roles of genetic makeup and lifestyles in the etiology of cardiovascular disease. A formal 5-year agreement between the U.S. Department of Health and Human Services (HHS) and the Israeli Ministry of Health for cooperation in the field of health was signed in January 1980.

In July 1975, the NHLBI established the Jerusalem LRC. One of its missions was to perform a prevalence study of dyslipidemia and its natural history in the Jewish population of Jerusalem. This LRC is the Israeli component of this prevalence study, and it capitalizes on Jerusalem's unique population mix. (In the study, 55 countries of origin are represented). The results show

important differences in blood lipid profiles that can be correlated with the country of paternal origin. Total cholesterol levels were lowest in teenagers of North African descent, highest in youths of European and Israeli origin, and intermediate in those from Asia. Triglyceride levels were lowest among North Africans, but Asian and Israeli groups had higher values than Europeans. Ischemic heart disease incidence and mortality in Israeli ethnic groups correlated positively with group mean total cholesterol values. Such strictly controlled international investigations provide important clues as to whether lowering blood cholesterol levels decreases the incidence of heart attacks.

The NHLBI also supports a joint American-Israeli Migrant Study of paired brothers or sisters, one of whom migrated to Israel and the other of whom remained in the United States. The study is designed to assess the role of genetic and environmental influences on cardiovascular risk factors. Analysis of the results is under way, and published reports are expected soon.

Poland

NHLBI cooperative activities with Poland operate under two separate mechanisms: the 1973 U.S.-Polish Agreement for Health Cooperation between the U.S. Department of Health, Education, and Welfare and Poland's Ministry of Health and Social Welfare; and the 1976 U.S.-Poland Collaborative Research Agreement supported by funds available under the Agricultural Trade and Assistance Act of 1954 (P.L. 83-480) and the Marie Skladowska Curie Fund.

The U.S.-Polish Agreement for Health Cooperation

At the first joint U.S.-Polish Symposium on Cardiovascular Diseases, held in the United States in 1978, representatives discussed a wide range of topics and gained a mutual understanding of the magnitude of cardiovascular disease in each country. Broad areas for cooperative activity were outlined, and a U.S.-Polish Cardiovascular Steering Committee was formed.

At a second U.S.-Polish meeting, held in Warsaw in 1979, three specific projects were identified for collaboration:

- Basic research on the mechanisms that regulate release of prostacyclin and other disaggregatory prostanoids in vitro.

- Clinical research on the diagnosis and treatment of cardiomyopathy and isotopic procedures for evaluating heart hemodynamics.

- Epidemiological research exploring the reasons for the marked differences in cardiovascular disease and trends in risk factors between Poland and the United States, with special attention to nutrition, hypertension, and smoking.

Joint work is proceeding in each of the above areas. The basic research on prostacyclin has been particularly fruitful during this period.

The U.S.-Poland Collaborative Research Agreement

Under the U.S.-Poland Collaborative Research Agreement, the NHLBI has supported two separate studies through the Marie Skladowska Curie Fund. The first is the Polish Trial in Multifactorial Prevention of Coronary Heart Disease, which is part of a European trial conducted under the auspices of the World Health Organization. The objective of the Polish trial is to screen approximately 18,000 middle-aged factory workers for cardiovascular risk factors (hypercholesterolemia, overweight, hypertension, smoking, and lack of exercise) and to investigate methods of intervention for these risk factors.

The second is the Followup Study of Chronic Nonspecific Respiratory Disease in Cracow. This in an NHLBI-sponsored 13-year prospective study, initiated in 1968, which is examining risk factors affecting the incidence, prevalence, and persistence of chronic nonspecific respiratory disease.

Federal Republic of Germany

A formal agreement was signed in 1976 between the U.S. Department of Health, Education, and Welfare (now HHS) and the Federal Ministry for Research and Technology of the Federal Republic of Germany (F.R.G.). Cooperative activities have focused on arteriosclerosis and hypertension and more recently on clinical trials. Initial discussions focused on the etiology, pathogenesis, and prevention of hypertension and arteriosclerosis. The two nations exchanged extensive information about current projects, and the F.R.G. representatives developed detailed proposals for joint studies based on ongoing collaborative activities. They discussed the need for standardized bioassays for important humoral cardiovascular control systems such as the renin-angiotensin system and for standardized assays for the plasma lipoproteins and apoproteins believed to be involved in atherogenesis. Standardization of methodologies would enable U.S. scientists to compare their data with epidemiological data from Germany and from other European countries as well.

Although the death rate from cardiovascular diseases in the Federal Republic of Germany has leveled off during the past 10 years, it has not declined. German scientists are interested in duplicating the marked decline in cardiovascular death rates seen in the United States in the last 15 years. The Federal Republic sent a delegation to the Institute's 1979 Conference on the Decline of Coronary Heart Disease Mortality and sent a representative to the U.S. National Conference on Hypertension held in the same year to learn more about the factors responsible for this improvement. With the aid of NHLBI experts, the Federal Republic established the "Bluthochdruck Ausbildungs und Fortbildungs Program" (High Blood Pressure Detection and Prevention Program), which is patterned after the U.S. National High Blood Pressure Education Program. Pilot studies are currently under way.

In Heidelberg in April 1981, the United States and the Federal Republic held a joint workshop on Multiple Risk Factor Intervention Trials. Workshop participants addressed areas including: intervention in unselected populations; evaluation for cardiovascular intervention; hypertension programs; and recommendations for German-American cooperation. The Heidelberg workshop was followed by a workshop in Munich that focused on epidemiology and preventive medicine and on hypertension control in community-based prevention programs. The two nations agreed to consider cooperative activities, based on the workshops, in the following areas during the next 2 years:

- Internationally comparable surveillance and monitoring of cardiovascular morbidity and mortality and their association with risk factors and health practices.

- The development and exchange of techniques and strategies for intervention studies.

- The development and exchange of techniques for evaluation and validation of approaches to intervention.

At the October 1981 meeting of U.S. and F.R.G. experts, discussions focused on the detailed methodology of the F.R.G. National Health Survey.

Future plans under the agreement call for the following additional activities:

- A joint analysis of the proposed German National Health Survey and Multicenter Intervention Trial with a special focus on standardizing the methods and procedures for laboratory research, electrocardiography, health behavior assessment (including nutrition and use of health services), assessment of psychosocial factors, evaluation

of endpoints, and organization, management, and data handling procedures for multicenter trials.

- A joint workshop, scheduled for 1982 or 1983, on Advanced Methods in Epidemiology Related to Research in Prevention with particular emphasis on health surveys, community surveillance, and intervention trials.

- An advanced course in epidemiology taught in the Federal Republic by U.S. experts during 1982 and paid for by the Federal Republic of Germany.

Italy

The science agreement signed by the United States and Italy in 1967 provided a general "umbrella" for scientific cooperation, under which individual biomedical projects have been incorporated since 1970. The signing of the joint U.S.-Italy Memorandum of Understanding in 1977 provided a specific mechanism for the cooperation of U.S. and Italian scientists on programs to prevent and control cardiovascular disease. Program participants examined the roles of the three major risk factors--hypertension, hyperlipidemia, and smoking--and the marked differences in disease patterns in the United States and Italy. Formal cooperation began in 1978 with a series of joint symposia and working meetings. The purpose of these meetings was to exchange, review, evaluate, and compare U.S. and Italian information in specific areas and to develop exchanges of scientists in these areas. To date, four symposia have been held:

- Measurement and Control of Cardiovascular Risk Factors (1978). At this symposium, U.S. and Italian patterns of cardiovascular disease and risk factors and efforts to control cardiovascular disease in the two countries were compared. An Italian physician presented new data on the role of vasospasm in ischemia and sudden death. This work catalyzed joint research showing that coronary vasospasm may contribute to, or be responsible for, functional impairment of the blood supply to the heart and thus influence the relationship between coronary atherosclerosis, heart muscle ischemia, and angina pectoris.

- Prostaglandins and Cardiovascular Disease (1979). This symposium was on new findings about the role of prostaglandins in different types of cardiovascular disease. Participants in the symposium agreed that a better understanding was required of the role of prostaglandins in the normal functioning of the cardiovascular system and their possible involvement in certain disease states. They also agreed that the mechanism of action of certain drugs

requiring the presence of prostaglandins needed clarification and that certain prostaglandin derivatives, which may turn out to be potentially useful drugs, should be developed. A U.S.-Italian working meeting entitled Methodology and Training in Prostaglandin Research in the Cardiovascular Area was held in 1980 as a followup to the symposium.

- Nutrition and Cardiovascular Disease (1980). At this symposium, participants discussed questions relating to the role of nutrition in the development and prevention of cardiovascular disease. They explored U.S. and Italian data on nutritional patterns and differences in cardiovascular disease rates. Also, the participants discussed the extensive international data base on nutrition and cardiovascular disease and also the uses of such information in efforts to prevent cardiovascular disease. The role of nutritional factors in hypertension and hyperlipidemia was also considered.

- Methods of Noninvasive Diagnosis in Cardiovascular Disease (1981). Topics included: characteristics of atherosclerotic lesions as they pertain to noninvasive techniques, status and future trends of the technology, and validation and clinical applications of noninvasive techniques. The U.S. and Italian participants shared the results of studies and reviews in each of these areas.

Exchanges of U.S. and Italian scientists for joint work have resulted in important new findings. Studies have been conducted on the role of thromboxane in atherogenesis and on the role of the intact endothelium in the mechanism of action of certain antihypertensive drugs.

In another cooperative effort, intramural scientists of the NHLBI and colleagues from the University of Milan School of Medicine developed a novel method of respiratory support to treat acute respiratory failure in newborns and in adults. This method, apneic oxygenation, is being used with considerable success in a U.S.-Italian trial to treat patients with adult respiratory distress syndrome. In patients with only a 10 percent chance of survival, apneic oxygenation was started after all conventional treatment had failed. Breathing was stopped, the lungs were kept inflated with pure oxygen, and metabolic carbon dioxide was removed by an artificial lung. Most patients treated in this manner exhibited rapid improvement, and among the 34 patients treated thus far, there have been 25 long-term survivors.

Yugoslavia

The United States and Yugoslavia signed an agreement in May 1973 to encourage joint research on projects of mutual interest.

In one joint project, NHLBI and Yugoslav investigators (the latter from the Institute of Chronic Diseases and Gerontology) cooperated in a long-term prospective study of the epidemiology of cardiovascular disease in a large population of Yugoslav men. Over 11,000 men aged 35 to 62 years were examined in an attempt to relate changes in trends of CHD risk factors and the prevalence of CHD death to changes in the sociocultural environment. The key methods and criteria employed were comparable to those used in the U.S. Framingham Study. Analysis of the results is under way, and several joint papers have been published.

The same group of investigators is now beginning a new joint project, an epidemiological study of secular trends in CHD risk factors in Yugoslavia. The objective is to investigate trends in CHD risk factors and in the prevalence of CHD and to attempt to relate these changes to changes in the sociocultural environment. The Centers for Disease Control is assisting with laboratory standardization. Data from this study will be comparable to epidemiological studies of coronary heart disease sponsored by the United States and the World Health Organization.

Japan

The U.S.-Japan Umbrella Agreement in Science and Technology in Non-Energy Areas was signed in 1980 by the President of the United States and the Prime Minister of Japan. This agreement provides for collaboration in the study of cardiovascular diseases. The United States and Japan have a long history of successful informal cooperation in cardiovascular research; formal cooperation at the international level will build on these contacts.

Specific cooperative activities now being planned include studies of the nutritional control of hypertension and its sequelae, and extension of previous epidemiological comparisons of patterns of cardiovascular disease in the two nations. Joint U.S.-Japanese basic research on nutritional control of hypertension and on one of its sequelae, stroke, has been proceeding informally for more than 10 years. Both countries are interested in expanding these studies under the formal agreement.

Japanese scientists have developed new animal models for the study of hypertension. Researchers at Kyoto University developed the spontaneously hypertensive rat (SHR), which has been used at the NIH since 1969. In 1974, scientists developed a substrain of

the SHR that exhibits more severe hypertension and is stroke-prone (SHR-SP). Cooperative research using these animal models has led to better understanding of neuronal regulation of blood pressure, vascular structure, and the dietary factors that may influence the incidence of stroke. SHR-SP develop severe strokes on diets inadequate in protein. When fed an adequate diet, these rats still become hypertensive but do not develop stroke. Scientists in Japan are now also developing arteriolipidosis-prone rats for study of the etiology of atherosclerosis.

Investigators in Japan have recently shown the importance of dietary protein in the development of stroke in man and the importance of the ratio of sodium to potassium in the diet in the development of hypertension. Further work on the nutritional modulation of human hypertension induced by high-sodium intake is proceeding. Scientists are also testing a nutritional supplement rich in potassium chloride for use in borderline hypertension.

Japanese and U.S. researchers have developed predictive tests for hypertension based upon the properties of the red blood cell membrane. Even before the SHR's develop hypertension, the red blood cells of young SHR's show an increased permeability to sodium ions, lipophilic ions, and an increased plasma membrane fragility. Further joint work will seek to establish whether changes in the properties of red blood cell membranes indicate human susceptibility to hypertension before overt high blood pressure develops.

A joint report on the nutritional prevention of stroke has been submitted for publication, and a joint project, Experimental Studies and Dietary Prevention of Hypertension and Atherosclerotic Disease, is under way at the NHLBI and in Japan. The NHLBI and the Japanese Society for Promotion of Science supported this project for 1981 and 1982. Also, a major NHLBI publication, The 1980 Report of the Joint National Committee on Detection, Evaluation, and Treatment of High Blood Pressure, has been translated into Japanese.

The Honolulu Heart Program, a 10-year prospective study of coronary heart disease and stroke in over 8,000 men of Japanese ancestry living in Hawaii, commenced in 1970. The incidence of coronary heart disease and its mortality in the Japanese population of Hawaii was between the higher level found in a similar cohort living on the U.S. mainland and the lower level of a cohort in Japan. Stroke prevalence, however, was three times greater in the Japanese cohort than in the Hawaiian cohort. There was a strong inverse correlation between serum cholesterol levels and the incidence of cancer, particularly colon cancer, in the Japanese cohort. The 10-year reexamination of 2,000 of these men is now under way and is scheduled for completion in 1982. A 10-year disease incidence and mortality roster has recently been

completed. The risk factors, both positive and negative, underlying these changes in morbidity and mortality are currently being studied.

Future plans under the U.S.-Japanese agreement call for continued exchanges of information on the epidemiological and experimental aspects of hypertension, periodic joint meetings, and the exchange of scientists.

People's Republic of China (Mainland)

Informal contacts between the United States and the People's Republic of China (P.R.C.) started in November 1978 when a Chinese delegation of cardiovascular scientists visited the NHLBI for a joint symposium on cardiovascular disease. Visits by delegations and individual scientists established other informal contacts. Formal cooperation began in January 1979 with the signing of the agreement between the U.S. Government and the Government of the People's Republic of China on Cooperation in Science and Technology. A subsequent protocol, signed in June 1979, identified cardiovascular diseases as one area for cooperation. A plan for collaborative studies in the cardiovascular area was developed during a visit by a U.S. delegation to China in April 1980 and was approved by the U.S.-P.R.C. Joint Health Committee in November 1980.

Cardiovascular epidemiology was selected as the initial topic of cooperation because it is by far the area of greatest mutual interest; cardiovascular disease is currently the leading cause of death in China and in the United States. There are important differences, however, in the patterns of the disease in the two countries, and study of the differences may yield valuable clues in understanding the etiology and prevention.

A delegation of Chinese specialists visited the United States in March 1981 to review scientific studies in progress in both countries and to participate in a joint workshop on arteriosclerosis and hypertension. At that time, specific plans for future cooperative activities were formulated. A four-member working group of U.S. cardiovascular specialists visited China in April 1981 to initiate discussions on the proposed U.S.-Chinese epidemiological studies of cardiovascular disease and its risk factors. U.S. and Chinese scientists formulated a draft protocol for epidemiological studies of urban and rural populations in North and South China. The protocol includes standardized techniques of measurement and data collection. Joint analyses of epidemiological data are planned. The protocol has been reviewed by both countries, and completion of the final protocol is expected during 1982.

Under the terms of the formal U.S.-Chinese agreement, two Chinese exchange fellows came to the United States from March 1981 to March 1982 to undertake research on the biochemistry of atherosclerosis and cellular studies of the pathogenesis of human atherosclerosis. In addition to these fellows, the Institute has also hosted a number of Chinese exchange fellows in the cardiovascular and pulmonary areas under the sponsorship of the Pan American Health Organization.

Future U.S.-Chinese collaboration will include completion of the protocol for the joint epidemiological study. Exchanges of information and scientists are also expected to continue.

France

Cooperative research by NHLBI and French scientists is conducted under the aegis of two agreements: the NIH-Institut National de la Sante et la Recherche Medicale Agreement signed in 1970, and the NIH-Centre National de la Recherche Program for Scientific Collaboration.

Interstitial Lung Diseases

In 1980, intramural researchers of the NHLBI and their colleagues at the Institut National de la Sante et la Recherche Medicale initiated a 3-year cooperative study of interstitial (fibrotic) lung diseases. This U.S.-French exchange program was established to share scarce patient biopsy materials. The exchange made it possible to undertake a variety of large-scale pathologic studies.

The combined research has led to several new findings. The incidence and significance of Langerhans cells in the lungs of more than 100 patients with various types of pulmonary fibrosis, for example, have been studied, and the results were published in 1981. Work on hypersensitivity pneumonia and histiocytic disorders has also been completed, and the results were presented at a major international conference. Other joint projects now under way include: a general review and revision of the criteria for the diagnostic classification of interstitial lung disorders on the basis of histological and electron microscopic findings, studies of the ultrastructure of Langerhans cells in histiocytosis S, studies of pulmonary ultrastructure in sarcoidosis and other diseases in which granulomas develop in the lung, ultrastructural studies of the pulmonary vasculature in interstitial lung disease, and studies of the morphology of abnormal collagens found in diseased lungs.

Serum Lipids

A U.S. physical biochemist spent 8 months at the Centre National de la Recherche, Center for Molecular Biology, studying the mechanisms by which serum lipids and apolipoproteins interact to form the stable native lipoproteins that circulate in the blood. The results of this research provided further insight into the atherogenic process and the protective role of high density lipoproteins against atherosclerotic plaque formation.

United Kingdom

During the past 10 years, the NHLBI has cooperated directly with the United Kingdom on two major projects: the development of a chemical information system and an epidemiological study of British-Norwegian migrants.

Chemical Information System

In 1971, scientists from the NHLBI Division of Intramural Research began cooperating informally with British investigators in the development of a computer-based chemical information system (CIS). The system includes analytical programs to accomplish iterative analysis of complex nuclear magnetic resonance spectra, general curve-fitting linear regression analysis, mathematical modeling, chemical synthesis programs, and many other specialized data bases. The data bases for the system were assembled by the NIH, the Mass Spectrometry Data Center (within the Department of Industry of the British government), the U.S. Environmental Protection Agency, the U.S. National Bureau of Standards, and several other U.S. Government agencies, as well as by private organizations and groups from the United States and other nations. As more groups and countries became involved in the project, it became necessary to adopt agreements governing patent rights and the use of data. Two international agreements were also signed that govern the exchange of spectral data with countries of Eastern Europe and the international pooling of nuclear magnetic resonance data.

This valuable information system, which contains 30 specialized data bases, is being made available to scientists in North America and Europe by means of an international teleprocessing network. During 1981, 14 countries cooperated in the further development of the CIS. These nations include Australia, Finland, France, Germany, the Netherlands, Hungary, Japan, Poland, Sweden, Switzerland, the United Kingdom, the U.S.S.R., and Yugoslavia.

British-Norwegian Migrant Study

A comparison of the cardiorespiratory morbidity and mortality of British and Norwegian migrants to the United States with that of British in Britain and Norwegians in Norway has been under way for some time. An analysis of mortality differentials due to coronary blood vessel disease, expressed as angina pectoris, was completed and reported at a major symposium in March 1981.

The study of angina pectoris was based on a mail questionnaire completed by 73,884 men and women in the United States, Great Britain, and Norway. The prevalence of angina and other symptoms was ascertained for each of the study groups. Contrary to expectation, angina was reported much more frequently by persons remaining in Britain and Norway than by the migrants to the United States. Review of mortality rates during the 5-year period following the questionnaire indicated that angina was a strong predictor of cardiovascular mortality. In the absence of angina, the migrants had mortality rates similar to those of nonmigrants regardless of country of origin. The British, however, had higher mortality rates from cardiovascular and from noncardiovascular causes than the Norwegians. Migration status was the primary determinant of angina prevalence; it is thought that this differential was primarily a function of those who migrate, with the migrants to the United States being a healthier group than those who remain in their native country. Work continues on assessing the effect of other cardiorespiratory symptoms and cigarette smoking on mortality differences between the migrant and native populations.

Venezuela

A U.S.-Venezuela science and technology agreement was signed in October 1979, and the U.S. Public Health Service and the Venezuelan Ministry of Health signed a Memorandum of Understanding for Health Cooperation in 1980. Joint discussions have been held to implement cooperative efforts under these agreements. Venezuelan scientists have a strong interest in cooperation in cardiovascular medicine, focusing on epidemiological and clinical research. Possible collaboration on cardiovascular aspects of Chagas' disease is being explored. Venezuelan and NHLBI investigators are developing a protocol for a prospective study of this disease that could potentially provide a human model of cardiomyopathy.

A cross-cultural study of lipid levels in school children has been conducted outside the formal cooperative mechanism. Data on children aged 7 to 12 from the Lipid Research Clinics were compared with data on private and public school children in Venezuela. Male-female comparisons within Venezuelan schools

showed lipid and lipoprotein patterns similar to those of U.S. children. For each sex, cross-cultural comparisons revealed two major differences: Venezuelan children had significantly higher fasting plasma triglyceride and lower HDL cholesterol levels. Venezuelan and U.S. public school children had remarkably similar total cholesterol and low density lipoprotein levels. Venezuelan private school children had significantly higher total cholesterol and HDL and LDL cholesterol levels than the public school children. They were heavier, taller, and ate a diet higher in total calories, fat, carbohydrates, and protein. Venezuelan private school children also had somewhat higher total cholesterol and LDL cholesterol levels than public school children in the United States. It is speculated that if these cross-cultural patterns are maintained, the risk of coronary heart disease and subsequent mortality in Venezuela may increase or converge toward the higher U.S. rate. (The coronary heart disease mortality rate for Venezuelan men is now slightly over one-half that reported for U.S. men.) Further analysis of these data is in progress.

Others

In addition to the programs described above, the NHLBI has developed worldwide contacts with many health officials and scientists. Many of these officials have visited the United States for joint discussions of health policies of mutual interest. Also, cooperative multinational activities have been initiated in several areas related to the Institute's mission. A sampling includes:

Nigeria

In July 1980, the Permanent Secretary of the Federal Ministry of Health visited the NHLBI with a delegation to discuss cardiovascular diseases. An NIH-Nigerian Task Force meeting was held in early 1981, and the Agreement for U.S.-Nigeria Cooperation in Biomedical Research was signed later that year. Cooperative activities are planned in the cardiovascular disease area, with emphasis on hypertension, and in the hemoglobinopathies, especially on sickle cell anemia.

Other African Nations

Scientists from the Sudan and Tanzania have visited the NHLBI and expressed interest in cooperative projects in the area of hypertension. Several African scientists were working on hypertension-related research in the United States during 1981.

Kuwait

In March 1981, the director of the Kuwait National Health Planning Office visited the NHLBI to discuss programs in the prevention of cardiovascular disease, and in May 1981, the U.S.-Kuwait Technical Cooperation Program in Health was signed. Kuwait, which is developing a national health plan, is seeking consultant help under this agreement to develop a national high blood pressure education program patterned after the NHLBI programs. The Kuwait Ministry of Health is also seeking such help with epidemiological studies and followup monitoring of the population after intervention. A senior Kuwaiti epidemiologist recently visited the NHLBI to discuss the U.S. Framingham Study.

Egypt

The NHLBI has participated in the work of the U.S.-Egyptian Joint Subcommittee on Biomedical Research, which was established under the Agreement on Health Cooperation signed in 1974. The Egyptians have submitted several proposals for NHLBI consideration. Prominent Egyptian cardiologists have visited the NIH in recent years to learn more about specific programs and areas of investigation.

Hungary

The 1977 agreement between Hungary and the United States on Cooperation in Culture, Education, Science and Technology was renewed in December 1981. The Hungarian Deputy Minister of Health visited the NHLBI in 1980 to begin planning activities in the cardiovascular area, and during 1981, the Deputy Director, NHLBI, visited the Hungarian Institute of Cardiology to continue this planning process. Plans are under way for exchanges of scientists for joint work.

Spain

The Treaty of Friendship and Cooperation between the United States and Spain is in the final stages of negotiation. Health is one of the areas specifically identified for future cooperation, and proposals for collaboration have been formulated in the areas of cardiovascular research, blood banking, and blood resources.

Greece

NHLBI and Greek scientists have been collaborating for many years on studies of the epidemiology of atherosclerosis and of the hemoglobinopathies, particularly thalassemia (Cooley's anemia).

The Pacific Basin

In January 1982, the NHLBI conducted a multinational workshop on the epidemiology of cardiovascular disease in the Pacific Basin. Scientists and observers representing Japan, Taiwan, Niue, Rarotonga, Philippines, Hawaii, Micronesia, Australia, New Zealand, Fiji, Nauru, Western Samoa, the People's Republic of China, the United Kingdom, and the United States attended this workshop, held in Hawaii. NHLBI epidemiologists have also cooperated in studies of the effect of migration on the familial aggregation of blood pressure of Tokelau islanders who migrated from an atoll in the South Pacific to New Zealand. This collaborative multidisciplinary study is focusing on the changes in blood pressure and other variables important in cardiovascular disease.

Romania

NHLBI and Romanian scientists are collaborating in research on von Willebrand's disease and its relationship to CHD.

Jamaica

A cooperative study on coagulation problems in sickle cell retinopathy is under way.

Pakistan

The president of the Pakistan Medical Research Council visited the NHLBI in 1980 to explore opportunities for cooperative research.

Argentina

The collection of human urinary erythropoietin is taking place in Argentina. After purification, it is distributed by the NHLBI for use as a reference standard in hematopoietic research.

The NHLBI responds to numerous inquiries from scientists throughout the world regarding publications on heart, blood vessel, lung, and blood diseases. One specialized NHLBI program that has generated international interest is the Primary Reference Materials program for hemocompatible materials to be used in cardiovascular prostheses. French, West German, Dutch, Japanese, Chinese, and Soviet researchers working in the biomaterials area have requested these reference materials, which will be distributed by the end of 1982.

The NHLBI also contributed to the support of a U.S. medical science expedition to Mount Everest. One purpose of this expedition was to record data on respiratory and cardiac function at high altitudes. Climbers at elevations of between 24,000 and 29,000 feet exhibit symptoms similar to those of emphysema, chronic bronchitis, respiratory failure, and myocardial infarction, all of which can result from inadequate blood oxygen supply to the organs and tissues. Analysis of data from the expedition is under way.

In addition to the many scientists who visit the NHLBI under bilateral agreement programs, there are approximately 40 visits each year by delegations and individuals from other countries throughout the world. These are usually national policymakers and senior administrators who visit the Institute to discuss national health policy questions.

During the past 10 years, Institute representatives have participated in hundreds of international meetings on all facets of medicine, ranging from basic science to clinical subjects. The meetings provide an opportunity for NHLBI staff to join international colleagues to exchange information on the latest advances in medicine and science.

The NHLBI also receives many international scientists for joint work in its intramural laboratories. During the past 10 years, 531 scientists from 38 countries have participated in this program. The majority of these scientists have come from Japan, India, the United Kingdom, Italy, Israel, Canada, Taiwan, Sweden, Brazil, and the Federal Republic of Germany. The number of visiting scientists from each nation is listed in table 4.

Scientists from many countries are contributing to the NHLBI National Program. During fiscal years 1972 to 1981, funds were awarded for 168 projects undertaken by foreign scientists in areas directly related to U.S. priorities in the Institute's mission. The countries receiving contracts and grants from the NHLBI and the countries where U.S. scientists have received fellowships for training are listed in table 5.

Table 4. Visiting Scientists
National Heart, Lung, and Blood Institute
Division of Intramural Research
1972 to 1981

Australia	4	Ireland	5
Belgium	3	Israel	32
Brazil	16	Italy	42
Cameroon	2	Japan	118
Canada	25	Korea	3
Chile	3	Luxembourg	3
People's Republic of China	1	Netherlands	1
Colombia	1	New Zealand	10
Czechoslovakia	2	Norway	2
Denmark	7	Pakistan	1
Finland	2	Poland	8
France	8	South Africa	5
Germany (Federal Republic of)	12	Spain	7
Greece	1	Sweden	21
Hong Kong	1	Switzerland	4
Iceland	1	Taiwan	24
India	84	Turkey	4
Indonesia	1	United Kingdom	63
		Venezuela	1
		Yugoslavia	3

Cooperation With International Organizations

Over the past decade, the NHLBI has cooperated with a number of international organizations, particularly with the World Health Organization. In 1978, the Director, NHLBI, was appointed advisor to the WHO for long-range planning of programs in cardiovascular disease. As noted previously, the WHO designated the NHLBI in 1980 as a Regional Collaborative Center for Research and Training in Cardiovascular Diseases for the Americas. In this capacity, the NHLBI provides advisory services to the WHO and collects and exchanges information on cardiovascular diseases. The exchange includes data pertaining to all facets of disease control, from results of basic research to epidemiological studies, and data from prevention and control activities.

Institute staff members have participated in many meetings, workshops, and specialized committees sponsored by the WHO and have acted as expert consultants on a wide range of topics. In the area of hypertension, Institute staff have served on the Mild

Table 5. National Heart, Lung, and Blood Institute International Programs Fellowships, Contracts, Grants Fiscal Years 1972 to 1981

	Number	Funds Paid (in dollars)	Countries	
Fellowships*	90	$ 751,291	Canada	Italy
			Denmark	Japan
			Federal Republic of Germany	Netherlands
				Norway
			Finland	Sweden
			France	Switzerland
			Israel	United Kingdom
Contracts	79	17,762,613	Canada	
			Israel	
			Japan	
			Netherlands	
			United Kingdom	
Grants	99	3,941,592	Argentina	Italy
			Australia	Japan
			Austria	Lebanon
			Belgium	Netherlands
			Canada	New Zealand
			Denmark	Nigeria
			Finland	Romania
			France	Sweden
			Greece	United Kingdom
			Ireland	Uruguay
			Israel	
Total	268	$22,455,496		

* To U.S. scientists for postdoctoral training in foreign research institutions

Hypertension Liaison Committee established in 1975 by the WHO and the International Society of Hypertension. The purpose of this committee is to exchange information on the progress and characteristics of worldwide pilot trials in mild hypertension. Institute staff members have also participated in meetings on a cooperative hypertension control program sponsored by the WHO in 15 centers around the world. In 1979, NHLBI staff provided material for the report of the WHO Expert Committee on Arterial Hypertension. NHLBI staff members have also served as WHO consultants on hypertension research.

In 1979, the U.S. Coronary Artery Surgery Study and the European Coronary Surgery Study began exchanging data, using the WHO as the coordinating agency. The NHLBI has also been cooperating with the WHO on Myocardial Infarction Registries.

The NHLBI has collaborated with the WHO on epidemiological studies and on prevention and control programs in cardiovascular disease. Expert consultants identified by the NHLBI assisted Thailand, India, and Bangladesh in WHO-sponsored national planning in the cardiovascular area. The Institute provided a senior consultant to the WHO to aid in the analysis of data from a 17-country study on the prevalence of cardiovascular disease in patients with diabetes.

Using its extensive knowledge of risk factors in cardiovascular disease, the NHLBI continues to be involved in establishing comprehensive WHO programs for the nonpharmacological prevention and control of chronic noncommunicable diseases. A panel of 20 international experts, which included two NHLBI scientists, drafted the provisional protocol for a new monitoring system to measure the incidence of ischemic heart disease in the WHO-sponsored study, Multinational Monitoring of Trends and Determinants in Cardiovascular Disease (MONICA). Pilot studies in selected communities are now under way. Data from this study will enable a more accurate assessment of trends in heart disease morbidity and mortality.

Through its bilateral agreements with various countries, the NHLBI is indirectly involved in WHO-sponsored clinical trials. Poland, for example, is a participant in the European Multifactorial Prevention Trial coordinated by the WHO. By adding a few features to this trial, Poland and the NHLBI have been able to compare Polish results with data from the U.S. Multiple Risk Factor Intervention Trial. Furthermore, by taking advantage of Poland's participation in the WHO Community Surveillance Study, both countries are planning to collect comparable Lipid Research Clinics information to gain additional insight into the cardiovascular disease problems of both countries.

The NHLBI has coordinated the placement in U.S. research laboratories of a number of WHO fellows from the People's Republic of China to receive appropriate research training. A number of these fellows have worked in the NHLBI intramural laboratories.

A WHO consultant from Great Britain visited the NHLBI in 1980 to assist the Institute in developing a program of research in specific heart muscle diseases (cardiomyopathies). Seven grants were subsequently awarded for animal model studies of the etiology and fundamental mechanisms of these diseases. The studies have strong potential for a collaborative program.

In addition to its collaborative efforts with the WHO, the NHLBI cooperates with the Pan American Health Organization in exchanging information and providing expert advice and scientific review of plans for cooperative activities in Latin America and the Caribbean.

The NHLBI is currently working with the Commission of European Communities (CEC) in the area of extracorporeal oxygenation. Institute staff members are working with the European Concerted Action on Extracorporeal Oxygenation to exchange information about ongoing research on how to "transplant" the most up-to-date developments in engineering design, coagulation problems, and control systems as they relate to long-term respiratory support therapy. The European countries participating in this project are Denmark, France, the Netherlands, the United Kingdom, and the Federal Republic of Germany. Information has been exchanged regarding the CEC Concerted Action on Common Standards for Quantitative Electrocardiography. Researchers from the United States, Canada, and Japan as well as from the CEC countries collaborated to develop the protocol for this study. The Institute also assisted in developing the International Bone Marrow Transplant Registry organized by the CEC.

The International Organization of Legal Metrology (IOLM) has a subgroup on Instruments for Biomedical Measurement. An NHLBI member of this subgroup participated in the development of international IOLM standards for electrocardiographs, cardiac monitors, electroencephalographs, and rheoplethysmographs. Participating countries included the United States, the U.S.S.R., the Federal Republic of Germany, and the German Democratic Republic.

The Future

More than ever before, medical science is international in scope and character, and the potential of the NHLBI international programs is almost unlimited. There are many opportunities, and

constraints are primarily those of resources and skilled personnel. By making full use of international resources in science and medicine, the Institute can create an even stronger base for future development of the National Program. The Institute also hopes to strengthen its leadership in international research on cardiovascular, lung, and blood diseases and blood resources.

Despite the downward trends in cardiovascular mortality, U.S. death rates from premature coronary heart disease are still among the highest in the world for men and women (see figure 2). A serious new problem is emerging--deaths from pulmonary disease have increased markedly. To help solve these national health problems, the NHLBI plans to continue and to pursue the following international activities:

- Identify the areas of greatest promise for international collaboration in relation to the NHLBI national goals and program needs, particularly in the areas of epidemiology, prevention, and control of disease, and new approaches to therapy.

- Focus resources for international cooperation in areas of mutual interest and benefit--namely, the major problems in cardiovascular diseases and the increasing problems in lung diseases. Also explore opportunities for cooperation in blood diseases and blood resources.

- Honor current collaborative commitments and encourage new developments in high priority areas as resources and funds are available.

- Develop linkages with other nations in order to encourage cooperation in research and cofinancing of programs of mutual interest.

- Develop the cooperative planning processes initiated during the past 10 years, as described in figure 3, in order to provide the benefits outlined in figure 4 for the United States and other cooperating nations.

Through the Institute's international programs, U.S. scientists have an opportunity to learn about the organization, technology, approaches, and values of the scientific and medical enterprise throughout the world and to apply this knowledge to the planning and implementation of the NHLBI National Program. The citizens of the United States and other countries benefit from this cooperative international process by the elimination of less effective therapies and the redefinition of health problems; by the refinement of present treatments to make them more effective; and by the development of new approaches to the prevention and treatment of heart, blood vessel, lung, and blood diseases. In

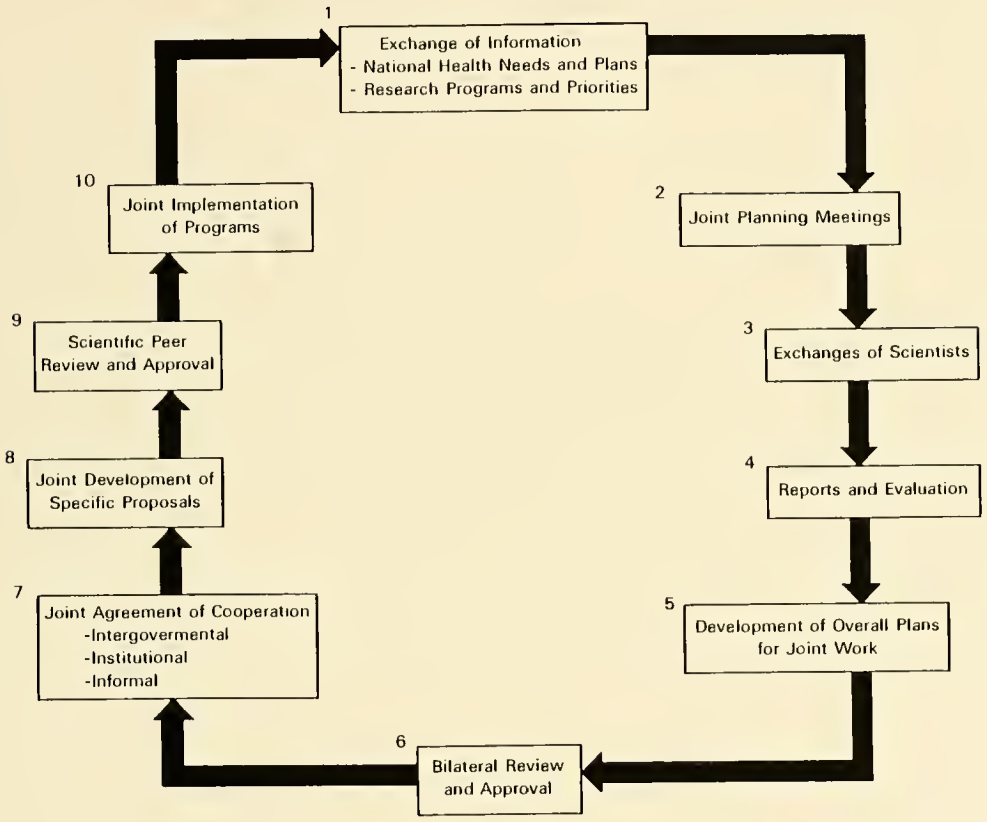


Figure 3. Framework for International Cooperative Activities

these ways, the Institute's international programs benefit not only the U.S. National Program but also contribute to the achievement of the WHO goal of "Health for All by the Year 2000."

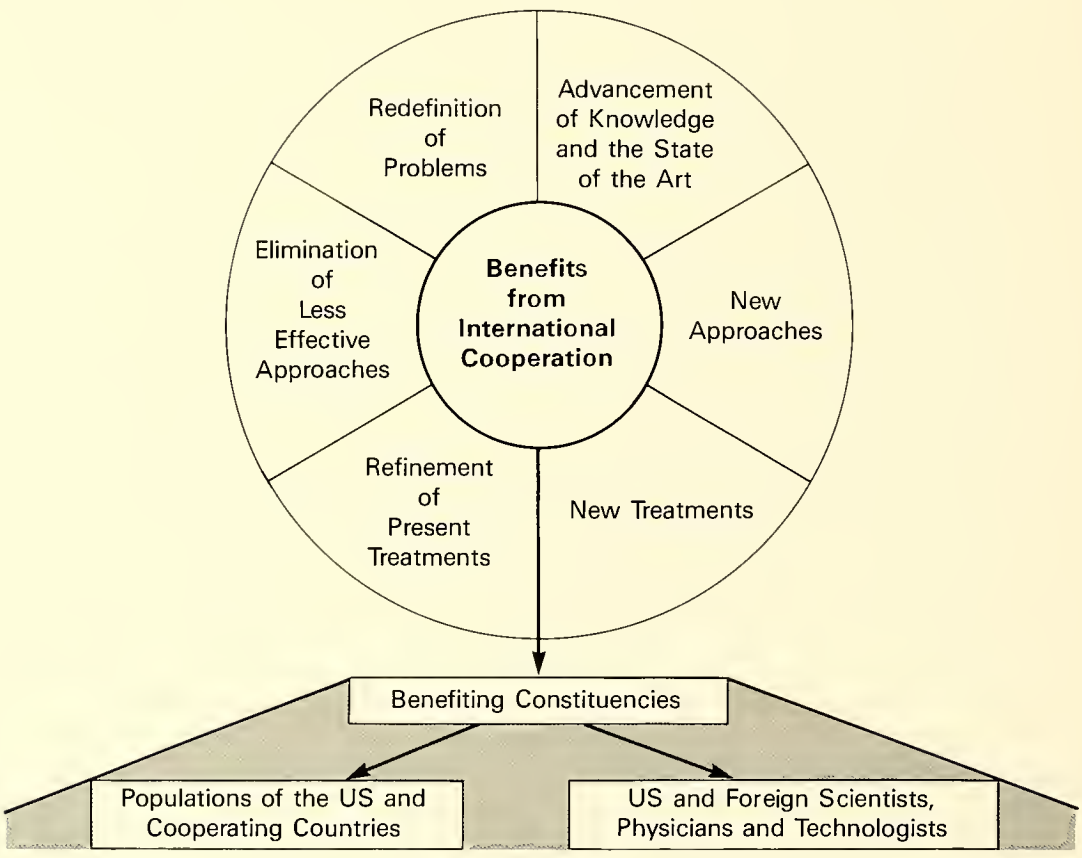


Figure 4. Benefits From International Cooperation

4. Research Training and Development

Contents

4. Research Training and Development

During the past 10 years, there have been major advances in the prevention, diagnosis, and treatment of heart, blood vessel, lung, and blood diseases. The advances have resulted directly from strong programs in basic, applied, and clinical studies. The research findings that led to the advances came from scientists working in nearly every conceivable discipline on fundamental and clinical studies--from physics to pharmacology and from biochemistry to epidemiology.

The continued strength of biomedical research in the United States depends in large part on a continuous supply of human resources. The availability of such resources is in the form of expertly trained biomedical and behavioral scientists, and it is in part ensured by fellowships, training grants, and career development grants administered by the National Institutes of Health (NIH). In the last 10 years, the National Heart, Lung, and Blood Institute, through a multifaceted array of programs, has continued its commitment to the training of talented biomedical and behavioral researchers in areas of shortage. Mechanisms used by the Institute include training grants, fellowships, minority training programs, programs for new investigators, research career development programs for clinical and academic investigators, and faculty training and curriculum development efforts for minority institutions and for scientific areas heavily in need of additional scientists. The NHLBI training program is interwoven with the broad training goals of the NIH as a whole.

Background

Today's complex array of NIH training programs has developed gradually. The Ransdell Act of 1930 (P.L. 71-251) established the NIH and included provisions for fellowships for duty at the NIH and other medical and research institutions. In 1937, the first major fellowship program was launched with the establishment of the National Cancer Institute. In 1944, the Public Health Service Act gave the NIH additional, broad legislative authorization for fellowships and research training.

After World War II, the NIH developed programs to respond to an increasingly obvious shortage of scientific personnel. Until 1946, individual grants were awarded for postdoctoral research

fellows and clinical traineeships for physicians to improve their capability in diagnosis and therapy. In 1946, existing programs were expanded to include predoctoral research fellowships. As new Institutes came into being, they modeled their training efforts after the program of the National Cancer Institute.

Undergraduate training grants were established in 1948. In 1950, the NIH modified this mechanism for use at the graduate level. The focus of training programs gradually shifted from clinical specialties to research and faculty needs, and the importance of clinical training under NIH sponsorship diminished.

Part-time fellowships were offered in 1954 to attract potential researchers early in their careers. Such training often took place during the summer or off-quarters. In 1957, a program was established to permit medical students to spend a year in research between their preclinical and clinical years. In addition, medical schools were encouraged to develop experimental approaches to identify, select, and train medical students for academic careers. In the late 1950's, a broad authority for training programs was enacted. Various programs were developed, applicants for grants competed nationwide, and grant recipients were selected by peer review.

In 1960, general research support grants made flexible funds available to medical institutions and permitted the NIH to discontinue postsophomore and part-time fellowships. When the general research grants were discontinued in the 1970's, short-term training awards were reinstituted, by Section 472 of the Public Health Service Act, as part of the national research service award (NRSA) training program to provide a 3-month structured research training experience for students in health professional schools.

In 1961, the NIH developed the research career award program by combining several senior research fellowship programs. The purpose of the program was to provide additional training for young, promising researchers in the beginning of their career and to enable established scientists to devote their time fully to their research activities. In 1964, the senior scientist component of the research career award program was phased out, but the research career development award was continued. Other types of fellowship and research training grants continued to evolve to meet changing needs of research training.

The administration determined that existing training authorization should be phased out in 1973, and that needs could be met through the private sector. After discussion in the scientific community, the academic community, and the administration, a new program of fellowships to individuals and to institutions was announced. In 1974, the National Research Services Act

was passed, which abolished all previous training authority and substituted individual and institutional NRSA training grants, including the senior fellowship which, in 1980, replaced the special fellowship that had been abolished in 1974. The individual fellowships and institutional training grants made under the NRSA support the majority of NHLBI postdoctoral training.

Various special focus, non-NRSA programs have augmented training and development opportunities at the NIH. In the mid-1970's, the young investigator research grant was introduced, and it later became the new or special investigator research award. This program funds meritorious research for relatively inexperienced investigators. The clinical investigator award, initiated in 1980, was intended to stem the decline of the number of clinicians in the biomedical research field.

In addition, several programs have been initiated to encourage minorities in biomedical and behavioral research. These programs include Minority Access to Research Careers, Minority Biomedical Support, Minority Hypertension Research Development Summer Award, and Extramural Associates.

Evolution of Programs

The research training and development efforts at the NHLBI in large part mirror efforts at the NIH, with a special focus on the availability of scientists needed for research on the diagnosis, prevention, and treatment of heart, blood vessel, lung, and blood diseases. The National Heart and Lung Advisory Council recognized the relevance of training to research activities by stating in the 1972 National Program:

> Supply of skilled manpower is an essential element in a national effort designed to advance the attack upon heart, blood vessel, lung, and blood diseases. An adequate long-range plan in an expanding program directed against these diseases will require an expanding manpower pool to conduct research and to replace skilled manpower lost through attrition.

The Council stressed the need to strengthen existing training programs, provide continuing support, and encourage investigators to explore new areas of research. To achieve such goals, the Council recommended support for professional research groups and a variety of training and development awards and research fellowships.

Since then, annual reports of the Director of the Institute have recorded the efforts to reach the goals presented in the

National Program, including goals concerning human resource development. In the early reports, emphasis was placed on making personnel development an integral part of a whole that includes research and health care. The Institute also emphasized proceeding in an orderly fashion in the development and implementation of training programs to fill the many needs in rapidly expanding disciplines, from bioengineering and microcirculation to biochemistry and hemoglobinopathy. By 1975, it became apparent not only that the existing pool of researchers and educators needed replenishing but also that new and unique specialty needs were emerging that required a new training focus. Special emphasis was placed on filling personnel needs in the blood banking science and in interdisciplinary approaches to thrombosis, biomaterials, and hemoglobin research. At the same time, the Institute was fully aware that meeting personnel needs would be a lengthy process and that trainees could not be expected to contribute fully to the activities of the National Program for a while to come.

Also in 1975, the Institute augmented its training programs by increasing or expanding research training opportunities for minorities. This development signaled the beginning of the NHLBI's long-standing participation in the Minority Medical Support Program and the Minority Access to Research Careers Program.

In the Fourth Report of the Director (1977), the Institute expressed concern about the decline in the number of training positions. By 1978, the total number had decreased by 19 percent since 1971 and had not paralleled the continuously expanding mandate of the Institute. Additionally, there was concern over the anticipated decline in the number of trainees in 1979 as a result of fiscal limitations imposed by a continuing resolution based on 1978 funds.

At the time of the Sixth Report of the Director (1979), disincentives for trainees included lagging stipend levels, payback requirements in the NRSA programs, tax liabilities of NRSA awards, and a general instability of funding for research training. To offset such disadvantages and to stem the decline in the number of trainees, the Institute developed new programs such as the clinical investigator award to provide additional incentives for talented scientists to focus their efforts on research.

Summary data were presented in the Sixth Report of the Director. The total number of full-time training positions (FTTP's) was 1,352. The number of physicians in training programs had decreased from 630 in 1972 to 295 in 1978. In response to the continuing training needs, the Institute developed further plans to augment and more closely focus its training and development programs.

Reflecting on its efforts for over a decade to provide training and career development for talented investigators, the Director concluded in his Eighth Report (1981) that, while

> intensified competition for limited financial resources at all levels of government has led to the concept of "stabilizing" the base of biomedical research project grants, even if it means a reduction of training in the next generation of basic and clinical investigators, simple logic provides that without research all scientific exploration must cease, but that research training itself is the key to accomplishments.

In 1982, concerns about training and career development stem from the results of repeated constraints on programs in past years, from limitation of funds due to a continuing resolution, and from a general leveling-off of research funds. Moreover, it has become increasingly difficult to attract qualified applicants in some of the programs, since new as well as experienced researchers are often sought by private industry.

In the following discussion, a distinction needs to be made between the number of individuals being trained, the number of training awards, and full-time training positions. Training programs provide direct support to individuals for either full- or part-time training, or they support an institution's program, where funds can be distributed, through the institution, among full- and part-time trainees. The total number of awards, the number of individuals trained, and the number of full-time training positions are all measures of the level of support for research training and development activities.

Figure 5 (Dollars Expended by the NHLBI on Research Training and Development, 1971 to 1982) reflects the fluctuation of funds over the last decade as a result of administrative and budgetary decisions. While there was an increase from $24.53 million in 1971 to $36.98 million in 1982, the real dollars diminish when they are adjusted for inflation.

Figure 6 (Full-Time Training Positions, 1971 to 1982) shows an increase in person-years from 1,577 in 1971 to 1,917 in 1982, as recommended by the Advisory Council. The exact number of total recipients in 1982 will not be final until July 1983, when the last awards for 1982 will be confirmed and accepted. Prior experience shows that the estimated numbers should not vary significantly from actual numbers. Thus the increase in full-time training positions means that, over the last decade, there has been a significant increase in the number of full-time positions for training and development despite level funding (adjusted for inflation), in part because of lagging stipends and decreased allowances to institutions.

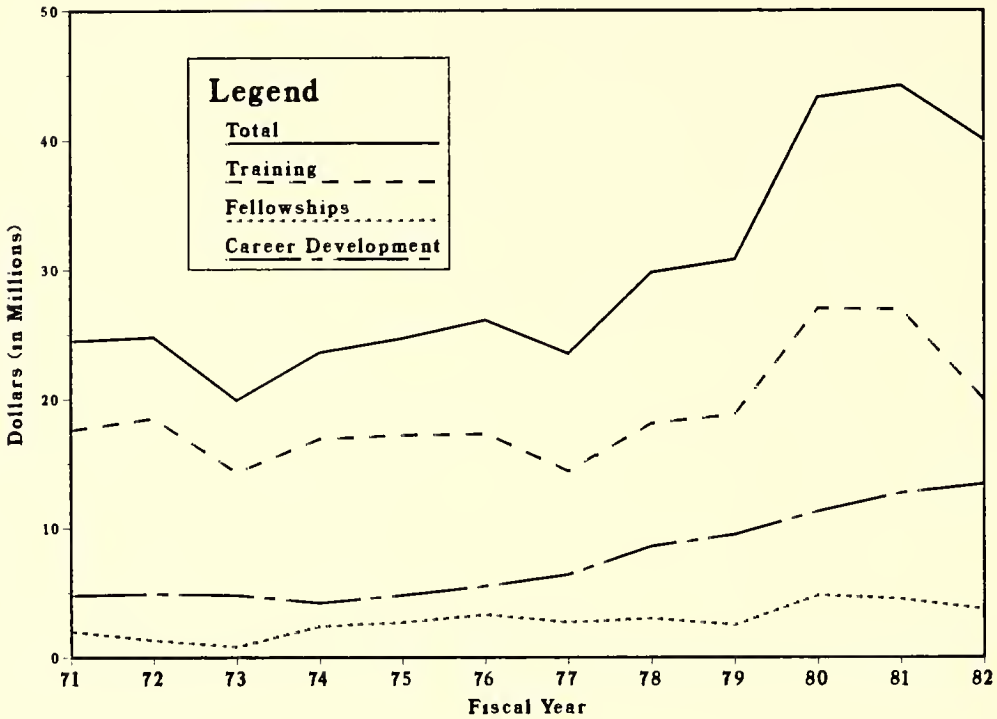


Figure 5. Dollars Expended by the NHLBI on Research Training and Development, 1971 to 1982

Figure 7 (Number of Full-Time Training Positions, Predoctoral and Postdoctoral, 1971 to 1982) shows that the number of full-time predoctoral trainees increased substantially from 264 in 1971 to 424 in 1982. A review of individual programs, however, discloses that the increase is caused by short-term, full-time, summer and off-semester training programs that were implemented in 1980. The number of postdoctoral, full-time training positions increased slightly from 1,234 in 1971 to 1,493 in 1982. This increase was due largely to an increase in career development awards from 182 in 1971 to 315 in 1982, and it reflects the implementation of new programs, such as the pulmonary academic award, the clinical investigator award, and the fuller development of the pulmonary career development awards.

Figure 8 (Number of Full-Time Training Positions, MD's and PhD's, 1971 to 1982) shows the relationship of the full-time

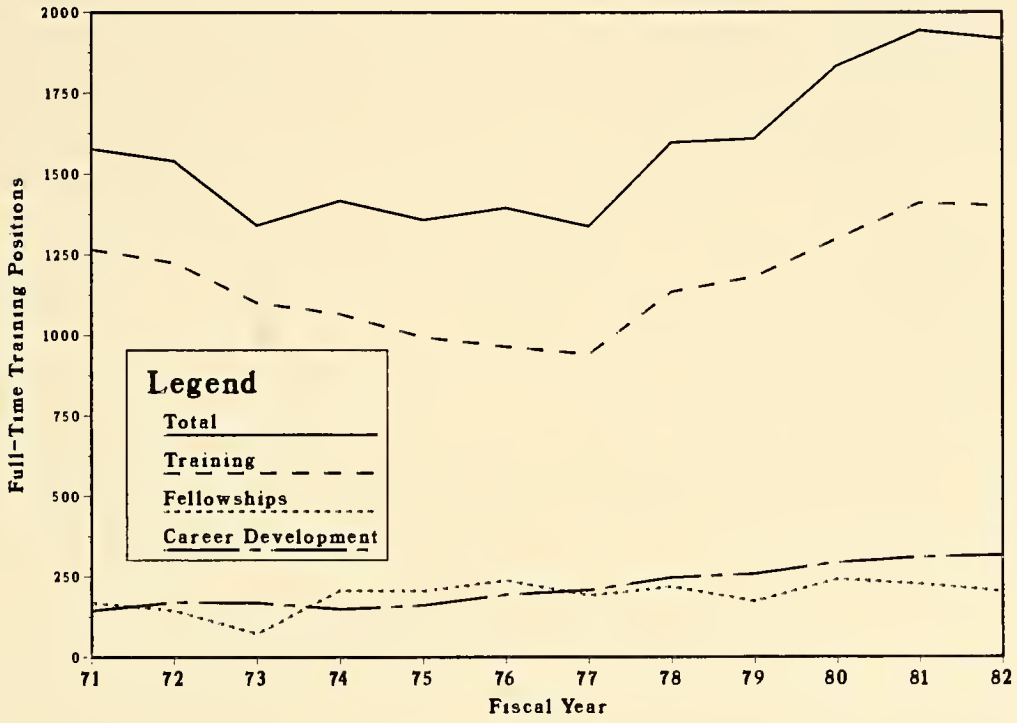


Figure 6. Full-Time Training Positions, 1971 to 1982

training positions of MD's to the full-time training positions of PhD's in the training and development population. (For statistical purposes, DDS's, DO's, DVM's, MD's, and individuals having both PhD and MD degrees are included in the MD category.) In 1971, there were 897 MD's and 337 PhD's. The Institute attempted to stem the decline of the number of MD recipients of awards by increasing the flow of program information to the clinical community and by instituting special focus programs, such as the clinical investigator award. In 1982, the ratio is expected to be 787 MD and 706 PhD FTTP recipients of awards. These numbers show progress in the attempt to increase the participation of MD's in NHLBI training and career development programs.

Projections for training and development in 1983 are expected to show maintenance of FTTP levels in research training and career development programs. The Institute is working to increase its interaction with other Federal health-related training programs to ensure optimal utilization of all available opportunities.

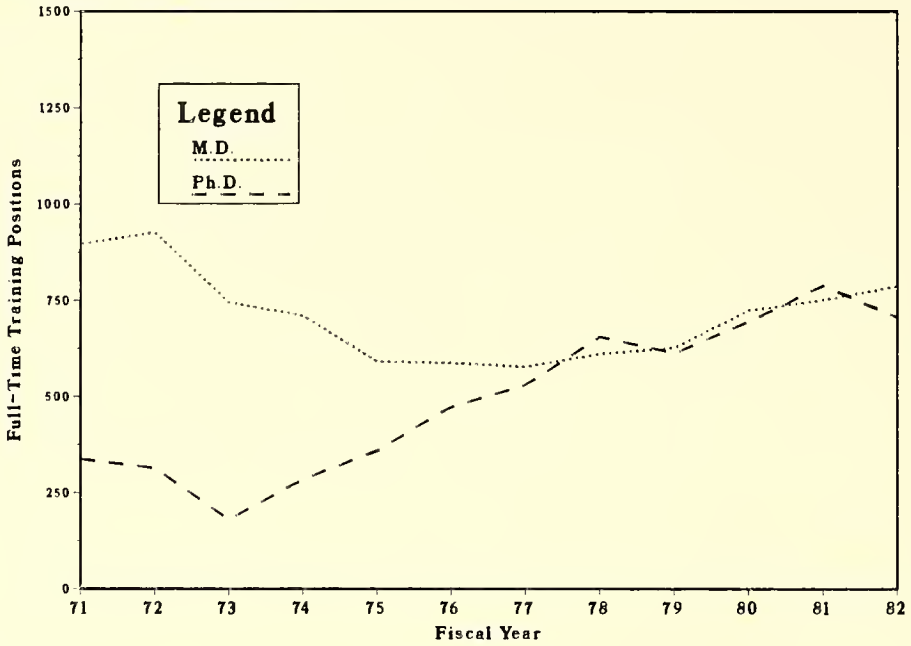


Figure 7. Number of Full-Time Training Positions
Predoctoral and Postdoctoral, 1971 to 1982

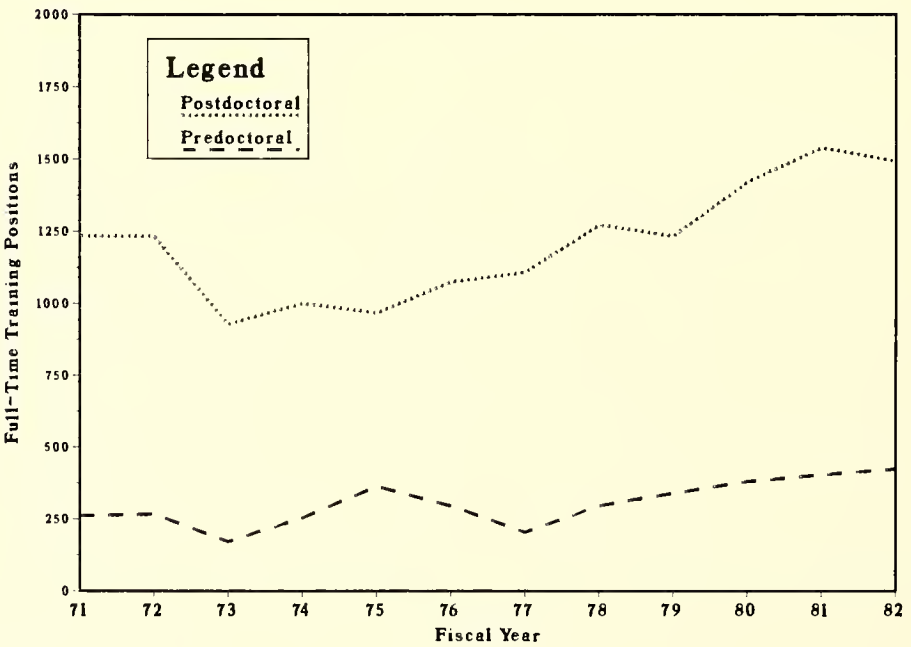


Figure 8. Number of Full-Time Training Positions
MD's and PhD's, 1971 to 1982

National Research Service Awards

The National Research Service Awards Programs, authorized by Section 472 of the Public Health Service Act, provide for short- and long-term awards to individuals as well as to institutions to produce qualified researchers in areas needing trained personnel. Research areas in need of skilled scientists are determined by an appropriate independent organization or component thereof, such as the Research Council of the Commission on Human Resources.

NRSA's support most of the research training and development activities at the NHLBI. Promising individuals are supported through training grants, fellowships, and minority training programs. In addition to training postdoctoral fellows in specified areas of biomedical and behavioral research, the NRSA programs provide support to institutions to develop or enhance research training opportunities. NRSA's, whether given to an individual or to an institution, permit persons with outstanding potential or proven research ability to direct or redirect their skills and interests towards biomedical or behavioral research in areas of concern to the National Heart, Lung, and Blood Institute.

Approximately 15 percent of NRSA funds are used to support qualified, promising individuals at different stages of their professional development. To qualify for an individual fellowship, the applicant selects a sponsoring institution that will provide appropriate facilities and supervision for a distinct research activity. After a sponsor is identified, the individual prepares an application for submission and competitive review by the National Heart, Lung, and Blood Institute. Competitions, which are national, are held at various times during the year. Applications that are accepted are assigned a priority score by the Council. The Institute then funds accepted applications in priority order within the limits of available funds. While applicants may be burdened with a cumbersome and lengthy process that takes 6 to 8 months, they enjoy the advantage of more independent research than most institutional awards provide.

Approximately 80 percent of NRSA funds are awarded to institutions, which, in turn, utilize these funds to provide their own training programs and research opportunities. Research-oriented institutions compete nationally for these awards at various times during the year. The recipient institutions are selected by the National Heart, Lung, and Blood Advisory Council. After receiving an award, the institution is required to appoint a program director and to develop its own review process for individual applicants.

In order to be considered for an individual appointment by a grantee institution, the applicant directly contacts the program director at the institution. Individual appointments can be

renewed annually, provided that a trainee's performance is acceptable and that the institution's training grant continues to be funded.

Programs guided by the principles of the NRSA include built-in, periodic reviews of stipends and institutional allowances, and they usually permit or encourage supplemental funding from non-Federal sources. They also limit any individual recipient to a maximum of 5 years of predoctoral and 3 years of postdoctoral support. Recipients must be American citizens or registered aliens. Two years after support has been terminated, the trainee is expected either to spend a comparable "payback" time in a full-time position in which health-related research or teaching is the primary focus or, if such positions are not available, to provide health-related, alternative service. While a financial payback route exists, less than 1 percent of NRSA award recipients have used this approach. Possible revisions of payback provision are presently pending before the Congress.

Approximately 4 percent of NRSA funds are used for short-term training. Present NRSA short-term training programs seek to attract minorities in health professional schools, minority students and faculty interested in hypertension training, and qualified individuals in need of upgrading existing skills or acquiring new skills in a very short period of time. Payback of training lasting less than 3 months is not required. The following descriptions highlight individual fellowship grants to institutions, career development awards, and other training-related programs at the Institute.

Fellowships

Postdoctoral Individual National Research Service Awards

In 1982, the NHLBI funded 193 individual grants through the Postdoctoral Individual NRSA Program, totaling $3.5 million. This program provides postdoctoral training for individuals to broaden their scientific background and increase their potential for research in specific health and health-related areas. Training periods vary from 1 to 3 years, depending on personal needs and career opportunities of applicants, and have averaged slightly over 2 years. Stipends are graduated according to the NRSA stipend scale from $13,380 to $18,780, depending on relevant postdoctoral experience. Allowances to non-Federal institutions are $3,000 and to Federal laboratories $2,000 per individual per year to cover trainee costs.

National Research Service Award for Senior Fellows

The Senior Fellows Program was initiated in 1977 to attract experienced scientists who have had at least 7 years of related postdoctoral research or relevant professional experience. Through research training, award recipients can make major changes in the direction of their research careers, or they can broaden the existing scientific focus of their careers. Program participants can acquire new, additional research capabilities, they can develop interdisciplinary competencies, or they can take time off from regular professional responsibilities to conduct research in heart-, lung-, and blood-related areas. In 1982, four individual fellowships totaling $107,000 were awarded in this program.

Stipends, which are individually negotiated up to $30,000, do not include fringe benefits and depend on the sabbatical plan of the fellow's own institution. Allowances to non-Federal institutions are $3,000 per trainee and to Federal laboratories $2,000 per trainee. Normally, fellowships last 1 year and can be renewed up to 3 years.

Minority Access to Research Career--Faculty Fellowships

The Minority Access to Research Career (MARC) Program was initiated in 1977. In 1982, the National Heart, Lung, and Blood Institute doubled its number of appointments and funded five individual faculty fellowships under the MARC program, totaling $110,000. While recipients in the past had always completed their PhD degrees before being accepted into the program, 1982 marked the year when a predoctoral faculty member was first accepted into the program. The program provides research training opportunities to faculty members in institutions with a substantial minority enrollment either for completion of the PhD degree or for postgraduate research experience in health or health-related areas. While this program is coordinated NIH-wide by the National Institute of General Medical Sciences (NIGMS), the NHLBI endorses candidates with research interests within its purview. Applications are funded by the Institute in a priority order, and they are transferred to NIGMS for administration. Amounts for awards, which are individually negotiated, are commensurate with salaries at the recipient's own institution and have a ceiling of $25,000. Allowances to non-Federal institutions are $3,000 per trainee and to Federal laboratories $2,000 per trainee. Service payback is not required.

Training

National Pulmonary Faculty Training Program

In 1982, the National Heart, Lung, and Blood Institute supported six training centers for 17 junior faculty trainees through the National Pulmonary Faculty Training Program. This program was designed in 1975 in response to the Manpower Survey Committee. The purpose of the program was to increase the number of well-trained biomedical teachers in the pulmonary field and to provide role models for aspiring students with the ultimate goal of increasing the number of pulmonary researchers. In 1975, six National Pulmonary Faculty Training Centers were established through national competition, and in 1976, institutions lacking a strong pulmonary program were invited to nominate junior faculty for the medical school pulmonary faculty training award for training in one of the six centers. Institutions with strong programs in research and biomedical sciences are thus training junior faculty members from institutions wishing to establish or strengthen academic programs in pulmonary research. Awards provide support for 5 years, 3 years of which are spent in research and clinical training at training centers. The trainee uses the remaining 2 years to establish pulmonary programs at his or her own institution. Awards are commensurate with institutional salaries and are negotiated individually. Since the need for pulmonary specialists in most subspecialties is expected to be saturated in the late 1980's and since the program was considered to have achieved many of its objectives, the granting of awards was discontinued in 1982.

Institutional National Research Service Awards

The objective of Institutional National Research Service Award Programs is to enable institutions to make awards to individuals for predoctoral and postdoctoral research training in specified areas of shortage, such as hypertension-related research and blood transfusion sciences. In 1982, the NHLBI provided support totaling over $19 million to 209 institutions for 300 predoctoral and 960 postdoctoral research training positions. The institutional NRSA grants at the NHLBI support short- and long-term programs.

Stipends are awarded on a sliding scale, with predoctoral stipends at a minimum of $5,040 and postdoctoral stipends ranging from $13,380 for a new trainee to $18,780 for a trainee with 7 years of relevant postgraduate experience. Institutional allowances are up to $3,000 for each predoctoral trainee and $5,000 for each postdoctoral trainee in addition to 8 percent of

direct costs. Training periods are limited to 5 years for predoctoral trainees and 3 years for postdoctoral trainees.

Short-Term Research Training Programs

The Minority Hypertension Research Development Summer Award Program, initiated in 1977, is short-term training for faculty members and graduate students from minority institutions within 100 miles of centers. Individuals receive training in hypertension research, prevention, control, and education. Recruitment, nomination, and selection of trainees is conducted jointly by the hypertension training center and the minority institution. Stipends for this program are awarded on a sliding scale, depending on educational level and relevant experience, from a minimum of $5,040 for predoctoral trainees to a range of $13,380 to $18,780 for postdoctoral trainees per year. Tuition and fringe benefits, if documented and applied for, are included. Institutional allowances per year range from $1,500 per predoctoral student to $2,500 per postdoctoral student. The hypertension center is permitted to retrieve 8 percent of direct costs. Training is provided for 3 months, can be renewed for 3 years, and does not require service payback.

The short-term and summer research training program provides predoctoral students in health professional schools with exposure to research activities early in their training. The program provides training during off-quarters or summer periods for up to 3 months and encourages research careers in multidisciplinary clinical investigation. In 1982, the Institute supported 34 institutional grants that involved more than 560 students (4 to 32 students per year in each institution). Support is $420 for each student with an institutional allowance of up to $250 per month plus 8 percent of total direct cost, with allowable supplementation from non-Federal funds. Payback for training of less than 3 months is not required.

Career Development

Non-NRSA activities encompass career development programs to bridge for new investigators the transition from training to research, programs to provide an element of stability for award recipients in times of shrinking resources for research, programs to develop research capability and to expand the experience of clinical and academic investigators beyond specific research projects, and programs for special needs such as curriculum development and correction of personnel shortages in particular specialties.

Research Scientist Development Award

The Institute has participated in the special emphasis research career award (SERCA) in diabetes mellitus since the beginning of the program in 1978. This award provides the opportunity for a young clinician with research interest to acquire experience and skills in the broad fundamental and clinical scientific disciplines essential for a multidisciplinary approach to the study of diabetes mellitus. In 1982, the Institute provided support, totaling $413,000, to eight researchers in their efforts to develop a multidisciplinary capability with the focus on diabetes mellitus. Necessary qualifications included an MD or equivalent professional degree with at least 2 years of post-MD experience, or an MD-PhD degree combined with 2 years relevant postdoctoral experience. The award is for 5 years, is not renewable, and includes full-time salary commensurate with experience up to $30,000 plus fringe benefits. Non-Federal supplementation is allowed and is used by most recipients. Research support for the first 3 years is up to $8,000 per year and for the 4th and 5th year up to $20,000 per year.

Research Career Development Award

Through the Research Career Development Award (RCDA) Program, the Institute supported 155 individuals in 1982 and provided almost $6 million. The purpose of the RCDA program, which was initiated in 1961 and has been refocused several times, is to foster the development of young scientists with outstanding research career potential and plans in a productive research environment and to ease the transition into independent investigation. Applicants demonstrate their understanding of the difference that the award will make to their future careers and are expected to have at least 10 to 15 years of productive research activity beyond the program. The award, which is for 5 years and is nonrenewable, should be supplemented by non-Federal funds. The institution nominates individuals, provides facilities, and sees to it that awardees are free from heavy teaching loads, committee assignments, and administrative duties, so that at least 75 percent of their time can be devoted to research. The sponsoring institution is permitted an 8 percent allowance of total direct costs. Salary support matches the institutional salary level and fringe benefits up to $30,000. In addition, the awardee is expected to have other research support for at least 2 years concurrent with the award.

Research Career Awards

The Research Career Award Program enables institutions to finance research positions that facilitate intellectual growth and research productivity of established investigators of high competence for the duration of their careers. In 1982, the Institute supported 20 individuals for a total of $653,000, providing support up to $25,000 and fringe benefits and an 8 percent institutional allowance of direct costs. When it became apparent in 1964 that the overall benefits of the program no longer merited the costs, no additional awards were granted. The awards in existence at that time continue to be honored.

Academic Investigator Awards

The purposes of the Academic Investigator Award Program are to create and encourage an approach to curricula that will stimulate the interest of high-quality students and to foster the development of promising teacher-investigators early in their academic careers. In 1979, the preventive cardiology award was established to support faculty members who specialize in preventive cardiology in schools of medicine or osteopathy. The award is intended to attract outstanding students, develop senior faculty members, and develop an improved curriculum with local funds. By enabling the grantee institutions to strengthen their existing teaching programs, the awards also assist in the development and implementation of interdisciplinary arrangements. In 1982, the NHLBI supported 38 promising academic investigators with a total of approximately $2.3 million. Stipends, which range up to $30,000, are individually negotiated, are commensurate with institutional salaries, and require a research commitment of at least 50 percent of an investigator's time. Appointments usually last 5 years and are not renewable.

The Academic Investigator Award Program includes the pulmonary academic award, which was initiated in 1970. This program encourages students to pursue studies in respiratory medicine and diseases and provides senior staff for research and development in pulmonary disease curricula. To date, more than one-half of the medical schools in the United States have held pulmonary academic awards. In a 1980 evaluation, the Association of American Medical Colleges determined that the program had been timely and effective and had largely met its goals. It was subsequently recommended that the program be phased out. A second special-focus program is the preventive cardiology academic award. It was initiated in 1978 for the development of preventive cardiology curricula in schools of medicine and osteopathy that do not have such a focus and for strengthening and improving the preventive cardiology curricula in schools that do. It supports outstanding faculty members who show a commitment and possess

skills for teaching, research, and practice of preventive cardiology. To date, 14 persons have received awards.

Teacher Investigator Awards

The purpose of the Teacher Investigator Award Program is to provide an opportunity for promising medical scientists and faculty members to develop into independent investigators. The particular focus of awards under this program is to close faculty gaps in identified biomedical and behavioral areas of shortage and to attract clinicians. In 1982, the NHLBI supported 94 individuals for a total of almost $4 million.

The Teacher Investigator Award Program subsumes the Clinical Investigator Award Program, which was established in 1980, and the National Pulmonary Faculty Training Program, discussed earlier. The Clinical Investigator Award Program was developed to stem a general decline in the proportion of physicians seeking training and research support at the NIH. The intent of the program is to draw physicians into research careers at an early stage in their professional development, and to compete with the attractions of clinical practice. Physicians accepted into this program have completed their clinical training and must show a strong potential for a career in research. The program provides 5 years of support for a supervised research experience in a promising environment. In 1982, the Clinical Investigator Award Program supported 77 clinical investigators in the areas of pulmonary disease, thrombosis and hemostasis, red blood cell disorders, and cardiovascular disease for a total of $3.4 million. In 1982, the national pulmonary faculty training award continued support for 17 individuals for a total of $527,000. No new awards were made.

Training-Related Research Activities

In addition to NRSA training programs and career development programs, the NHLBI supports other activities that assist the development of investigators, such as training workshops, minority research support, extramural associate appointments, several staff fellowship programs, and programs to bridge the transition from trainee to individual investigator.

Training Workshops in Cardiovascular Epidemiology

The Training Workshop Program in Cardiovascular Epidemiology is a joint effort of the Council on Epidemiology of the American Heart Association and of the NHLBI. This is an annual, 2-week workshop, the primary goal of which is to offer 30 postdoctoral

health professionals engaged in teaching, research, and preventive programs an intensive orientation to cardiovascular epidemiology and prevention, and to attract junior participants into careers in cardiovascular epidemiology and biometry. The training faculty consists of cardiovascular clinicians, epidemiologists, and biometricians who have made outstanding contributions in research and teaching. Applications for training are solicited nationally, and information concerning the program is released through the American Heart Association and other organizations from the cardiology community. Focusing on attracting junior participants who have clinical skills but lack orientation and basic training in cardiovascular epidemiology and biometry, the core faculty reviews applications and selects participants.

Minority Biomedical Support

The Minority Biomedical Support Program is a cooperative effort between the NHLBI and the Division of Research Resources, NIH. This program is designed to strengthen the biomedical research and research training capability of minority institutions by encouraging research by minority faculty, students, and investigators. The NHLBI investment in this program increased from $113,696 in 1975 to $1,708,000 in 1982. While the program is not a training program in the strictest sense, it assists in establishing for faculty and students of minority schools a more favorable milieu in health-related sciences through encouragement of training.

Young, New, or Special Investigators Awards

By using NRSA and career development programs, the promising and relatively new investigator takes the initial steps towards achieving independent status as an investigator. The Young Investigators Award Program originated in the young investigator pulmonary research grant, which since 1974 has vastly extended the base for pulmonary research. In 1976, the program was reannounced for the NHLBI as a whole, and since then, it has been emulated by many of the other Institutes. Ultimately, the program was consolidated into a single, NIH-wide funding mechanism, the new investigator research award (NIRA). The NIRA is a first-time award that helps to bridge the transition from trainee to totally independent investigator and supports meritorious basic and clinical research. The award also ensures the active research involvement of investigators in the early stages of their careers. Principal investigators on NIRA grants are expected to provide the Institute with information on their scientific achievements and professional status for 6 years following the completion of the award. The Young Investigators Award Program originated in the young investigator pulmonary research grant, which since 1974 has

vastly extended the base for pulmonary research. In 1976, the program was reannounced for the NHLBI as a whole. It has subsequently been emulated by many of the other Institutes. Ultimately, the program was consolidated into a single, NIH-wide funding mechanism, the new investigator research award. In 1982, the Institute supported 225 such grants at a total of $10.2 million.

Applicants for this program compete nationally for assignments as principal investigators and receive priority ranking through review by the Council. Grants are funded in priority order within the existing budget. Principal investigators must have a doctorate at the time of award and must have no more than 5 years of research experience after the completion of their formal training. Also, applicants must not have been a principal investigator on a project supported by the Public Health Service and should not concurrently apply for research grants or research training or development grants. Awards, which are made for up to 3 years, are nonrenewable and are granted to the institution on behalf of the investigator. Salaries range up to $25,000, depending on research experience and extent of time to be spent on the research grant. Non-Federal supplementation is permitted. Total direct costs can include technical support, supplies, publication costs, limited equipment, and necessary travel, and should not exceed $37,500 for any 1 year, with a 3-year maximum of $107,500. Each principal investigator is expected to spend at least 50 percent of his or her time on research. Researchers are expected to be able to compete for regular research grants upon the completion of the award.

Extramural Associate Program

Senior staff of the NHLBI have actively contributed to the Extramural Associate Program as advisors and as lecturers. This program is administered by the Office of the Director, NIH, and reflects the NIH's commitment to ensure that minorities and women have an equal opportunity to participate in and contribute to medical research. Key administrators from schools that contribute significantly to the pool of minorities and women in science spend 5 months in residence at the NIH. Institutions nominate persons on their own staff and are reimbursed for salaries, travel, and other related expenses of the participant. Applicants are interviewed by an NIH-wide review group of senior science administrators, which recommends the most highly qualified applicants to the Deputy Director of the NIH for final selection.

Senior health scientists and health administrators from the Institutes, including the NHLBI, are assigned to the associate to assist in developing a curriculum tailored to the associate's strengths, interests, and needs. Curricula focus on onsite

information about Federal health-related programs and related grant and contract activities. At the end of the program, associates return to their own institutions to become a primary source from whom faculty and students can draw information on how to seek, obtain, and increase health research grants.

Staff Fellowship Programs

The Institute also participates in the NIH-wide staff fellowship programs. As of December 1982, the NHLBI supported 40 staff fellows and 4 senior staff fellows. The objectives of these programs are to strengthen research in the biomedical sciences by fostering a continuous exchange of talented scientists between the NIH and other research centers, and to create a reservoir of trained personnel for future service at the NIH and other research institutions.

In the staff fellowship program, investigators are appointed who have fewer than 3 years of research experience at the professional level. The senior staff fellowship program is designed to attract research investigators with 3 to 7 years of research experience at the professional level or are physicians with 3 or more years of specialty training. The fellowship stipend is determined by the candidate's educational and professional experience. The stipend levels are reviewed periodically, and adjustments are made to parallel the salaries and benefits of Civil Service and Public Health Service Commissioned Corps positions. Fellowship awards are made for an initial 1- or 2-year period. Normally, extensions of appointments are limited to a total service period of 4 years in nontenured status.

Medical Staff Fellowship Program

The NHLBI also participates actively in the NIH-wide Medical Staff Fellowship Program. This program provides physicians with training and experience in clinical and laboratory investigation. Positions in the program encompass medical specialties and basic science disciplines. Minimum eligibility requirements include completion of 2 years of graduate medical training before entry into the program. Applications are made 1 or 2 years before the desired time of appointment. Appointments are based on professional attainment, research interest, and ability. Potential staff fellows are interviewed by a committee composed of the director of intramural research, the clinical director, and the deputy clinical director of the Institute.

Each fellow participates in a research program under the direction of a preceptor from the Institute. After receiving an appointment, the fellow has an opportunity to select a suitable

research group. The level of research responsibility depends on the fellow's training and experience, with a primary focus on time spent on research. Training is augmented by coursework through evening courses offered by the graduate program of the Foundation of Advanced Education in the Sciences, Inc., and through NIH tutorials. Appointments can be made in the areas of clinical research, surgery, laboratory research, staff appointments, epidemiology, and endocrinology. The latter is a joint venture with the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases and the National Institute of Child Health and Human Development. The starting salary for medical staff fellows is $30,000 plus benefits comparable to Civil Service employees, with a $2,000 increase per year.

During the decade 1972-1982, the NHLBI provided more than $330 million in support of direct research training and development, career development, and other training-related activities, and it continues to express its commitment to the training of the Nation's future biomedical and behavioral scientists in cooperation with other Federal agencies, academic institutions, and private industrial and other organizations.

5. Legislative History

Contents

5. Legislative History

The National Heart Institute was established by the National Heart Act of 1948 (P.L. 80-655), which added a new section to the Public Health Service Act. Since 1948, the Congress has reauthorized and enlarged the Institute's mandate four times, including its expansion to the National Heart, Lung, and Blood Institute. These revisions have greatly increased its responsibilities.

1972 Legislation

Through the National Heart, Blood Vessel, Lung, and Blood Act of 1972, the Congress strengthened its commitment to the Institute and to research in its disease areas. The change of name from the National Heart Institute to the National Heart and Lung Institute was codified into statute, and several new sections of the Public Health Service Act gave the Institute additional responsibilities. To meet these responsibilities effectively, the Institute needed a new strategy. The law mandated that the Director of the Institute, with the advice of the National Heart and Lung Advisory Council, develop a National Program within 180 days of enactment. A thorough review was undertaken of the state of scientific research in heart, blood vessel, lung, and blood diseases. The review included the advice and comments of hundreds of experts in these fields, and it resulted in a comprehensive National Heart, Blood Vessel, Lung, and Blood Diseases Program for:

- Research into the epidemiology, etiology, and prevention of heart, blood vessel, lung, and blood diseases
- Research into basic cardiovascular biological processes
- Development and evaluation of techniques, drugs, and devices to aid diagnosis and treatment
- Programs to develop technological devices to assist, replace, or monitor vital organs
- Field studies and large-scale tests relating to those diseases

- Research into blood diseases and the use of blood resources in the United States, including such items as collection, preservation, fractionation, and distribution

- Education and training of scientists and clinicians

- Public and professional education programs in all aspects of those diseases

- Programs to research and study heart, lung, blood vessel, and blood diseases of children

- Programs to research and develop emergency medical services, including training of paraprofessionals and development of specialized equipment and communications.

The National Program, which is updated each year, has continued to be the foundation of the Institute's activities. In a provision of the 1972 legislation, Congress mandated that the Director of the Institute submit an annual report to the President, for transmittal to Congress, on the accomplishments of the National Program during the preceding year and on plans for the next 5 years. The act also mandated that the National Heart and Lung Advisory Council submit an annual report to the President, for transmittal to Congress. In addition, the Council was expanded from 16 to 23 members, and it included, for the first time, representatives from the general public and from medical residency training programs. Similar to the Institute's increased mandates, the Council's functions were expanded to encompass heart, blood vessel, lung, and blood diseases.

The 1972 Act also:

- Established a specific post of assistant director for health information, to provide the public and health professionals with information about cardiovascular and pulmonary diseases, emphasizing the effects of lifestyle factors such as diet, smoking, exercise, and stress

- Required the Institute to establish prevention and control programs with other governmental and private health agencies, with appropriate emphasis on children's diseases, and delineated authorization of appropriations for that purpose

- Authorized the establishment of up to 30 national research and demonstration centers (15 for heart, blood vessel, and blood diseases, and 15 for lung diseases, including lung diseases of children) to foster coordinated programs in basic and clinical research, training, and demonstration

- Established an Interagency Technical Committee, chaired by the Director of the Institute, to coordinate those aspects of all Federal health programs related to heart, blood vessel, lung, and blood diseases and blood resources

- Specified that a minimum of 15 percent of appropriated funds be utilized for programs in lung diseases and a minimum of 15 percent for programs in blood diseases and blood resources.

From 1948 until 1972, the Institute received appropriated funds under the general research authority of Public Health Service Act, Section 301, which has no specific disease category allocation or "time and dollar" limits. Beginning with 1972 legislation, Congress designated a specific authorization level and renewal period for the Institute. (Similar action had been taken in 1971 regarding the National Cancer Institute.) The 1972 act authorized 3 years of funding, and the Institute required reauthorization on June 30, 1975.

1975-1976 Legislation

Reauthorization legislation proceeded through Congress during 1975, was delayed into 1976, and was signed into law in April 1976. It provided for a 2-year renewal period, rather than 3 years, so that the next reauthorization would coincide with that of the National Cancer Institute and with publication of the President's Biomedical Research Panel Report. Reauthorization in the Health Research and Health Services Amendments of 1976 provided funding authority for fiscal years 1976 and 1977. (During this period, the beginning of the fiscal year was shifted from July 1 to October 1.)

The major feature of the 1975-1976 legislation was to emphasize, clarify, and expand the Institute's role in blood-related areas. Specific action included the following:

- Congress changed the Institute's name to the National Heart, Lung, and Blood Institute and changed the Council's name to the National Heart, Lung, and Blood Advisory Council.

- In the several Public Health Service Act sections where Institute responsibilities regarded "heart, blood vessel, lung, and blood diseases," Congress added language about "the use of blood and blood products and the management of blood resources."

- Blood diseases and blood resources were added to cardiovascular and pulmonary diseases, as areas of information dissemination, mandated for the Institute's Office of Prevention, Education, and Control.

- The distribution of up to 30 national research and demonstration centers was reorganized into 10 centers for heart, 10 centers for lung, and 10 centers for blood.

Committee report language showed that Congress intended the Institute to function as the locus of coordination for blood research programs and for research in the management of blood resources.

Other notable highlights of the 1975-1976 legislation included:

- A new authority for the Advisory Council, to recommend to the Secretary areas of research to be supported by contracts and to recommend the percentage of the Institute's budget to be expended for contracts

- Changes in requirements of the Director's annual report, to be submitted after the end of each fiscal year rather than calendar year and to include personnel and appropriations estimates for the following 5 years

- Changes in requirements of the Advisory Council's annual report, to be transmitted simultaneously to the President and Congress rather than to the President for transmittal to Congress and to be transmitted by November 30 each year rather than by January 31.

1977 Legislation

Because both Congress and a new administration were interested in undertaking a major review of all biomedical research authorities through extensive "biomedical overview" hearings and reports, the Biomedical Research Extension Act of 1977 was a 1-year renewal. Congressional hearings began a series of discussions of several substantive issues in the conduct and management of biomedical research, and the legislation was kept to as simple an extension as possible. In the 1977 legislation, Congress:

- Reaffirmed the need for an expanded, intensified, and coordinated National Program, as mandated in the previous authorizations.

- Included a few technical amendments clarifying the role of research and demonstration centers for blood, adding cost-of-living increases for the centers in general, and reassigning one ex officio Council membership space from the National Science Foundation back to the newly reestablished Office of Science and Technology Policy.

1978 Legislation

The Biomedical Research and Research Training Amendments of 1978 was the result of a compromise of two sets of concerns. From the perspective of "biomedical overview," for which several major issues were still being explored and future hearings were being planned, another 1-year simple extension renewal was desirable. From the perspective of needed stability of research funding and planning, a 3-year renewal period was proposed. The compromise reauthorized the Institute for 2 years (fiscal year 1979 and fiscal year 1980) and included several amendments to increase the effectiveness of its programs.

The most significant amendments affected the submission of reports and responsibilities for information dissemination:

- Transmittal requirements for the Director's report were changed to correspond to the Council report route and timing, so that the Secretary transmits both reports, by November 30 of each year, simultaneously to the President and the Congress.

- Language that was added to the existing mandates for information dissemination mandates required that dissemination occur "on a timely basis."

- Responsibilities were added, in the dissemination program of the Office of Prevention, Education, and Control, for "nutrition" (in addition to "diet") and "environmental pollutants."

- Research and demonstration centers were required to have programs of continuing education for health and allied health professionals and also information programs for the public.

Additional technical amendments included a reimbursement provision for experts and consultants.

1980 Legislation

The Health Programs Extension Act of 1980, which reauthorized the National Heart, Lung, and Blood Institute, was signed into law on December 17, 1980. It provided for a simple 2-year renewal period for existing authorities through September 30, 1982.

1982 Legislation

Authorizations of appropriations in the 1980 law expired on September 30, 1982. As of this writing, Congressional action on reauthorization is expected.

Ten-Year Review and Five-Year Plan

National Heart, Lung, and Blood Institute

Volume 1. Progress and Promise
NIH Publication No. 84-2356

Volume 2. Heart and Vascular Diseases
NIH Publication No. 84-2357

Volume 3. Lung Diseases
NIH Publication No. 84-2358

Volume 4. Blood Diseases and Resources
NIH Publication No. 84-2359

Volume 5. Companion Issues
NIH Publication No. 84-2360

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