EDITORIAL

The National Heart, Lung and Blood Institute: a plan for the eighties

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IN THE three and one-half decades since the National Heart Institute (now the National Heart, Lung and Blood Institute) was established under the 1948 National Heart Act, there has been spectacular growth in both the number and variety of research activities supported by the Institute to elucidate processes involved in the onset and progression of cardiovascular diseases, and to develop effective therapeutic and preventive measures for their control. With the passage in 1972 of the National Heart, Blood Vessel, Lung, and Blood Act, the Institute established its national program to address an expanded mandate. Under current legislation, the Institute's mission has three separate but interdependent research phases: knowledge acquisition, knowledge validation, and knowledge transfer. In addition, it supports career development and training of scientists, clinicians, and teachers in the subject areas within its mandate. It is now somewhat more than two years since the Institute, its advisory council, and members of its advisory committees recognized the need for a comprehensive review of progress since the passage of the 1972 legislation. In the very near future the Institute will issue five reports that will collectively constitute the "Ten-Year Review and Five-Year Plan" of the NHLBI National Program. They represent the efforts of 28 groups involving a total of about 250 experts who contributed to this important series of documents. The reports will be transmitted to the President and the Congress, and later to the biomedical community. The Institute will draw upon the recommendations in developing plans for consideration by its advisory committees and advisory council. The reports will also inform the public about the many benefits derived from the national investment in research.

The voices of the biomedical community reach us in various ways. Most recently it was through the enterprise of our advisory council, which held four public briefing meetings to inform biomedical scientists, administrators, volunteer health organizations, and the public about the status of the Institute and possible strategies for maintaining a balance among program mechanisms and to ensure that an adequate number of meritorious research grants are awarded. Through the questions and discussions at these briefing meetings, the Institute was able to learn directly the nature of the concerns of the biomedical community and its perceptions of what needs to be done to minimize problems in the future. A report on this undertaking will soon be released.

The history of the Institute provides many examples of the advantages of programs that allow scientists access to a variety of supportive mechanisms and research approaches and to select those most appropriate to a given scientific objective. Although the investigator-initiated research project grant is the most frequently selected option, program project and center grants as well as contracts for research and for clinical trials have met the needs of scientists whose work requires a collaborative effort. The Institute’s advisory council has enthusiastically endorsed and encouraged this use of multiple supportive mechanisms, and the use of investigative approaches ranging from basic to applied, to demonstration and education research. Similar views are succinctly stated in an article in the September 1982 issue of this Journal, in which Dr. Richard Remington identified areas in which "it is crucial that choices not be made." These choices include those between basic and applied research, between prevention and treatment, and between the need to know and the need to take action.

The Institute’s 10 year review provides ample evidence of past successes in improving the diagnosis and management of diseases with which it is concerned and these are tangibly reflected in recent reductions in mortality from heart attacks and strokes. But disease prevention remains the Institute’s ultimate — although still elusive — goal. Also in the September 1982 issue of the Journal, Dr. Eugene Braunwald expressed his own vision of the future: "Today's cardiology is the diagnosis and treatment of these conditions. Tomor-
row's cardiology will be their elimination. This will require a major rechanneling of our efforts into the fundamental life sciences."

The objective of disease prevention can only be realized if we expand our knowledge of causes and patho-genetic mechanisms by drawing on what the basic sciences have to offer. Having gained an understanding of how disease processes can be prevented or interrupted, we must bring these insights to physicians, other health professionals, and the public through the application of demonstration and education research.

It is now necessary to face the challenge of the eighties. This is a time when such basic-science fields as molecular biology, genetics, cell physiology, biochemistry, and experimental pathology can make great contributions if they can effectively be applied in studies of cardiovascular, lung, and blood diseases. It is also a time when we must face the realities of fiscal constraints unlike any in past years. We must look critically at what, in addition to money, has contributed to past successes, and we must ask what strategies should be developed to overcome problems we will encounter in the immediate and more distant future. This is a challenge we must face by working together as a community that includes government, academia, and industry and has in common the goals of disease control and prevention. As our technology has become more sophisticated, the Institute’s interests have come more and more to coincide with those of the business community. We are moving, albeit cautiously, to tap such nongovernment resources when cooperation will be of mutual benefit. We are also channeling our efforts with regard to knowledge transfer and education to establish similar relationships with volunteer organizations, which would enable us to bring the benefits of research to the community and the individual.

Program strategy

The following examples of recent advances in diagnosis, patient management, and prevention are illustrative of the Institute’s program strategy and representative of the scope, diversity, and interdependence of its research programs.

Advances in noninvasive diagnostic techniques for heart disease are reducing the risk (which is admittedly low) associated with intra-arterial angiography. Until recently this has been the definitive procedure for detecting and quantifying lesions in coronary arteries, but it is now being replaced by such noninvasive approaches as echocardiography, ultrasound, and emission tomography. Recent developments in echocardiography now permit a two-dimensional display of cardiac anatomy, an advance particularly valuable when applied to newborns to assess complex congenital defects. Ultrasound has the advantage of not being associated with any known hazards. Because no ionizing radiation is involved, patients may be reexamined repeatedly.

Specific radioisotopes are being used to visualize areas of infarction in the heart or areas of diminished blood flow. The technique is now being explored as a means of detecting plaque in arteries, with the use of a plaque-specific radioisotope label. Although the techniques of nuclear medicine are being routinely used in many institutions, research is still needed to identify specific radioisotope labels. Emission tomography, which is used to image radionuclides such as carbon-11, is improving resolution and sensitivity and making it possible to determine the size of an infarcted area, and potentially to determine the accumulation of plaque in arteries.

There have been impressive strides in both the surgical and medical management of coronary heart disease during the past decade. Some procedures performed in the catheterization laboratory for diagnostic purposes are now providing the basis for therapeutic intervention. The use of percutaneous transluminal cardiac angioplasty (PTCA) to widen the lumen of blocked vessels and the use of intracoronary infusion of streptokinase to dissolve thrombi are two especially promising alternatives to invasive surgical interventions. PTCA has been well established as effective for amelioration of single-vessel disease, and its use in multivessel disease is under investigation. Results of ventriculographic and coronary arteriographic studies in patients with myocardial infarction have provided the basis for the generally accepted notion that thrombosis is an important element in this acute event. However, long-term mortality rates have left unanswered the question of the relative efficacy of intracoronary and intravenous routes of administration of thrombolytic drugs. This question is now being addressed in a clinical trial. Investigators have recently combined the PTCA and streptokinase modes of therapy and found that PTCA can be safely performed after the intracoronary infusion of streptokinase. This approach is also being critically evaluated.

Among the most successful and widely known Institute initiatives is the prevention program addressing hypertension. It is now recognized in many quarters, including the Congress, as a model for an effective way to reach communities and to save lives. The program has emphasized the importance of detecting and treating high blood pressure as a way to prevent heart
attacks and strokes. Although we cannot claim that the dramatic decline in mortality from these diseases in recent years is a result of the high blood pressure prevention program, it is reasonable to assume that public education has contributed to this result. Implicit in the education and information programs is the belief that they can have a marked impact on lifestyles and the daily health practices of individuals. Therefore, these programs are designed to reach a broad audience that includes the general lay public, the medical and scientific communities, professional educators, and state and local governments. There is substantial evidence that large segments of the population are undertaking appropriate measures to control their blood pressure (figure 1), and that illness and premature death attributable to hypertension are declining.

The Institute also supports multicenter clinical trials when research findings suggest the efficacy of a therapeutic or diagnostic procedure but when its efficacy can be validated and safety assured only by controlled clinical studies.

Challenges and plans for the eighties

Hypertension and atherosclerosis are two areas of research that provide both challenges and promise, and that will have high visibility in the Institute's plans for the eighties.

Within recent years, researchers have come to perceive hypertension as a multifactorial problem in which neural, humoral, genetic, and environmental factors have interdependent roles. Neural control in particular is now recognized to have a much greater role in maintaining blood pressure than had been previously suspected and the use of techniques of neuroscience and molecular biology is contributing to our understanding of the mechanisms involved. It is now evident that lesions in specific areas of the brain can prevent the development of renal hypertension in the experimental rat model, but it is also clear that hormones are involved in the chain of events that results in hypertension. Although researchers are aware of such interrelationships, further study of the problem requires investigators not only conversant with blood pressure research but also with knowledge of neuroscience and molecular biology. Among the challenges is to provide the support, facilities, and training investigators need to take advantage of the information gleaned from the basic sciences, and to use this information to improve the control and prevention of hypertension.

The initiation and progression of atherogenesis involves numerous processes that can be studied by the methods used in molecular and cellular biology. It is too simplistic to view these processes, as is commonly done, in the broad terms of injury and repair. Recent research has established that the endothelium of arterial vessels has a primary role in atherogenesis, and has such diverse functions as the incorporation and digestion of low-density lipoproteins, production of various types of collagen, and elaboration of von Willebrand's factor, prostacyclin, and plasminogen activator, all of which are involved in blood clotting. Research on arterial endothelium is of the greatest importance because endothelium is involved in processes that lead to plaque formation. Because plaque formation is associated with proliferation of smooth muscle cells, biochemical studies are needed to elucidate these relationships.

Consistent with its effort to gain and disseminate new knowledge, the Institute will soon announce again its intent to support a limited number of National Research and Demonstration Centers (NRDCs). In 1975 the Institute established three such centers, one for each of its three divisions. The Institute's advisory council, which periodically reviewed the NRDC program, recommended that procedures for designating and supporting such centers be changed. As a result of extensive deliberations by the council and various advisory committees, as well as by Institute staff and members of the biomedical communities concerned with heart, lung, and blood diseases, the following concept of the NRDC emerged. As now envisioned, the NRDC is an enhancement of the Institute’s Special-
ized Centers of Research (SCOR) and demonstration and education research grant programs. The proposed approach will have the effect of stimulating rapid application of the results of laboratory, clinical, and demonstration and education research to the care of patients, the prevention of diseases, and the promotion of health. The new NRDC will merge and enhance both the SCOR and research and demonstration grant programs by adding a thematically related demonstration and education research component to a renewed or new SCOR grant.

In meeting the challenges of the eighties, the Institute will commit as much as is feasible to the support of investigator-initiated research, and will reduce as much as possible the internal costs of running the Institute. It must, however, be recognized that the years of spectacular growth in funding for biomedical research have ended, at least for the foreseeable future. We are prepared to face the need for new patterns of response. This means a concerted effort must be made to encourage physicians to enter academic careers and apply themselves to the fundamental and clinical research that must continue, with even greater emphasis on the fundamental investigations that are the key to the ultimate prevention of disease.

References
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