INTERVIEW WITH DR. DONALD S. FREDRICKSON

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BY STEPHEN P. STRICKLAND

IN HONOR OF

THE 100TH ANNIVERSARY IN 1987 OF

THE NATIONAL INSTITUTES OF HEALTH

and the

150TH YEAR IN 1986 OF

THE NATIONAL LIBRARY OF MEDICINE

OCTOBER 1986

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Introduction and Biographical Sketch

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This interview with Dr. Donald S. Fredrickson is one in a series of "oral histories" focusing primarily on the origins and development of the extramural programs -- most especially the grants programs -- of the National Institutes of Health, beginning with the establishment of the Division of Research Grants in 1946. Like Dr. Fredrickson, most of those interviewed had critical roles in the development of the extramural programs.

The grants program constituting the largest component of the NIH, the interviews also reflect judgments and perspectives about the impact of the grants programs on health and science.

Dr. Fredrickson first made an important name for himself as a clinical researcher, working of fundamental laboratory studies of the structure and function of the plasma lipoproteins, and subsequently gained the reputation of a splendid clinical director at the National Heart Institute. His name and reputation have since become even more important due to his having held three preeminent positions in the world of biomedical science: President of the Institute of Medicine of the National Academy of Sciences, Director of the National Institutes of Health and, currently, President of the Howard Hughes Medical Research Institute.

As Director of NIH, Dr. Fredrickson had the difficult challenge of presiding over that agency at a time when budgets were being held steady, rather than growing as they had in the preceding fifteen years, and at a time when the unquestioned health benefits of biomedical research were nonetheless being challenged on other bases, namely cost/benefit analysis and technology assessment and ethical questions about "the new biology" for which NIH-supported research had been very much responsible. He is widely credited with maintaining balance and progress, and undergirding morale at NIH during his six-year tenure, which reached from the administration of President Ford, through that of President Carter, and the first part of the Reagan Administration. The combined experiences of Dr. Fredrickson, as a bench scientist, a clinical director and holder of positions at the pinnacle of the biomedical research establishment in the United States, give him an almost unparalleled perspective.

This oral history project is being carried out, in 1986 and 1987, under a grant from the National Institutes of Health, administered by the National Library of Medicine.

STEPHEN P. STRICKLAND, PH.D. WASHINGTON, D.C.

Interview by Stephen Strickland with Dr. Donald S. Fredrickson

October 10, 1986

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SS: I am talking this morning to Dr. Donald Frederickson, President of the Howard Hughes Medical Institute, former Director of the National Institutes of Health, former President of the Institute of Medicine, and an old friend. We are talking about the role of NIH and the extramural programs in the advance of science and the creation of a network of scientific institutions and scientists that most people say puts America in the forefront of science in the world.

DSF: The federal government has had a remarkable effect on American universities in the last 40 years, creating the strongest system for academic scientific investagation in the world, and setting an international standard for graduate education in the sciences. The greatest share of this strengthening of institutions came through two federal actions. One was the GI Bill of Rights at the end of World War II. The other was the expansion and conversion of the NIH to the structure and position it has today. Since the early '60s more than half of the total government expenditures for research to the universities has come through NIH. For nearly 30 years it has been the mainstay of the careers for most biomedical researchers. About a third of its extramural expenditures of about \$4.5 billion per year also now goes to the universities to defray indirect costs of that research. If there be a touch of negative in these facts, it is the utter dependence that some universities today have upon this source of support.

SS: But that support has been remarkably stable over the long term, hasn't it?

DSF: It has. In 1981, it appeared that even NIH had peaked out -- and joined a period of decline in research support from all the other government agencies, except for defense. An "all-time" peak in NIH purchasing power seemed to have been reached in 1979. But NIH budgets today continue to rise and again seem to be keeping up with inflation. There has been some decline in particular areas of the NIH budget, but the support for investigator-initiated research remains relatively stable.

NIH Career and Inspiration

SS: We are talking about a period that more or less coincides with your thirty years in the federal government. That is, it was in the 1950s that the NIH really started coming into its own. The creation of new categorical institutes began in the late '40s and continued over a period of at least fifteen years. The extramural program itself began in earnest after World War II. Did these developments affect the career choices you made?

DSF: I decided to be a medical scientist when I graduated from medical school in 1949. A major question was how would this be possible financially. It was not until 1951 that I heard of the NIH as a vague but promising new creature rising in Bethesda. I went there to see if I could get a job. I was sent in to talk to a tall fellow sprawled behind a desk, and barely audible. His name was James Shannon. He was then Director of Intramural Research of the National Heart Institute. In a few years he would be Director of NIH and its leader during the period of its great expansion. Obviously neither he nor I had a clue then that I would someday occupy the job he then held and someday also become the Director. Our interview ended with my becoming one of twelve clinical associates who would be brought to Bethesda in 1953 to open the Heart Institute's beds of the huge Clinical Center. This research facility, which placed 500 beds in close proximity to 1000 laboratories, was to be the marvel of its age.

I had come from the Massachusetts General and the Peter Bent Brigham hospitals. Those are great institutions, but did not prepare me for what I found in Bethesda. There was in this sleepy suburb of Washington a density of talent, freedom of research and intellectual opportunity that may never be equalled. In this environment we young physicians were exposed to a highly critical atmosphere and left to prove what we could do, pursuing ideas that were often generated by contact with disease on the wards.

SS: This situation on the NIH campus was replicated, I take it, gradually throughout the country.

DSF: That's the interesting thing, Steve. For the first ten years there was nothing comparable to NIH, and "everybody" came to work there, not always with the approbation of their home institutions. I remember Walter Bauer, a Professor of Medicine at the Mass General, telling me in one of his blue funks how the NIH would be a "gigantic Federal backwater". Ten years later Bauer come to the "backwater" himself to recruit the talent which would be the next generation of the medical and basic science faculty at Harvard. So it went at most other schools.

It was also a powerful growth stimulant to NIH that its Public Health Service origin made it possible to allow a limited number of persons to serve selective service time at Bethesda, those early years extending from the military drafts for the Korean Conflict and Vietnam War. The time saved by those intending to follow careers in research was critical. Bethesda thus also became the repository of the scarce talent for providing the medical school faculties just as the "biological revolution" was about to begin. NIH cloned itself in the late '50s and early '60s. It is only quantitatively unique today; for the quality has been dispersed into a truly nationwide system.

Geographical Expansion of Research Excellence

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SS: Originally, when you came to NIH from Harvard, weren't most of the other clinicians also coming from there or comparable institutions? I'm trying to get a picture of the geographical expansion of biomedical science talent and the multiplication of good research going on in a variety of places.

DSF: In the beginning a network of professors in the big universities in the the Northeast was the major source of talent recruited. At that time, many of

the institutions around the country weren't sufficiently academic to contribute many. Take, for example, what is one of the top three medical schools in the country today, the University of California at San Francisco. In 1950 it was a pleasant haven for private practitioners. About that time, the late Julius Comroe (not an NIHer) migrated from Pennand led a very small cadre of scientifically minded people to get the assistance of the President of the University to bring a new dean. Thus was opened a channel through which new talent, many of them key people trained at Bethesda, could migrate. That story was repeated over and over again in the U.S. Thus, from the pools of Bethesda flowed a crucial number of young, well-trained people who would become the key researchoriented faculty members of every medical school in the country.

SS: This is such an important point. Could you give other illustrations of schools that have become "top flight" in the last 25-30 years which would never have been thought able to attain such status except for NIH?

DSF: Well, as another example, the new medical school in La Jolla was established with a sudden hemorrhage of staff from the National Heart Institute trickling westward after Eugene Braunwald. The University of Michigan, arguably long ago the foremost medical school in the nation, found its strength badly ebbing after the war, partly due to faculty inbreeding. It took an important group of people from NIH via Duke, led by William Kelley, to revamp the Department of Medicine and greatly strengthen the school.

An important metabolic cycle was also rising. The new schools or the newly refurbished ones would send some of their best back to NIH for further training. The cascade of people going to and from Bethesda started other clusters elsewhere. Soon there were widely scattered, rapidly growing clones of hard-minded, capable people who were being maintained in research by the burgeoning extramural programs of NIH.

Central Role of Grants Programs

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SS: So the extramural programs have been the pivotal factor in building the national biomedical science capacity?

DSF: Even though grants were being awarded by NIH in small amounts since at least 1937, the intramural program was the NIH shot that ignited the great chain reaction. Those who migrated to new institutions and other geographical areas were sustained by NIH research grants. Research support was rising almost faster than programs to use it could be created. In one of the most remarkable creations of government, Congress delegated the power and the responsibility to pick the scientists to be supported: Through study sections, there proceeded a remarkable phenomenon of the "consumers" deciding which of themselves merited the federal support. Although a few enterprising Congressional staff members tried to stir up trouble, there has never been a breath of scandal in this unique process.

SS: Can we divide the impact into two parts? In the first place, I take it that the NIH, through the grants program, has been helping to multiply scientific activity of very high quality wherever it might be carried out. In the second place, it has obviously impacted on particular institutions. Just on the science part, is there more to say about the impact?

DSF: Initially there was also money available for massive effort to attract large numbers of talented young people to do science, but money was also channeled into the creation of the institutional base, to the expansion of the universities and hospitals. There was a lot of money for construction. Centers rose and disrupted the old academic structure in many ways annoying to faculty, but with important effects on both interdisciplinary growth of the sciences and the application of new discoveries to treatment and prevention. There were even teaching programs for clinicians so that the quality of practice was quickly improved in certain specialties. The amount going to institutions in these other ways was kept secondary to research grant support in my time, as the number of research grants that could be supported became the calculus for assuring adequate increases in the budget.

Sources of Medical Science Advances

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SS: In talking about recent medical science advances, the most dramatic that I've seen described in the last couple of months have been related to the development of chemicals or drugs that might retard the AIDS virus and conditions associated with AIDS. NIH has been central to what seems to me to be very rapid progress against the hideous disease, but pharmaceutical companies have also been involved. Much less important but of interest to many people is Upjohn's development of a formula that might retard baldness and restore hair, thus putting spotlight on the private sector industry's advances. How does this reflect, if it does, the general state of scientific activity and knowledge?

DSF: Perhaps the generic lesson from this is that today's great pharmaceutical houses also have many star scientists who also came up through the NIH intramural or extramural system. The current Chief Executive Officer of Merck, which possibly has the largest research organization in the world, is now Roy Vagelos, who was a fellow clinical associate of mine at NIH. So was the present Director of Research at Merck. Present day research talent in the pharmaceutical industry has never been greater. Here again NIH has been the source of many of the present leaders.

SS: Is there any area of biomedical science that cannot be identified as having been fed in some way by the NIH experience and program?

DSF: It would be difficult to identify such an area. Of course, key discoveries come about in ways that are often hard to trace. You are aware of the tally sheets showing that over 60 of the winners of the Nobel Prize in medicine or physiology have been supported by NIH. With such a dominant role in keeping the labs lit, it is not surprising that so many discoveries can be traced to NIH in one way or another. This is not only true for medicine but for chemistry and early work on recombinant DNA technology in plants.

Effect on Institutions

SS: On the institutional side, when I was growing up in Birmingham, Alabama, steel and coal were the dominant industries. Today, the University of Alabama at Birmingham is the dominant industry, so to speak, and obviously that relates very much to the fact that medical school and dental school and other health science schools have flourished. This has also happened in a number of other places and the role of the NIH has been quite significant. My next question is

what effect the NIH grants program has had on institutions as institutions. Grants are a stable funding element in an institution, but what else have they done to institutions?

DSF: We have covered some of those effects earlier. The nature, indeed the very origin of NIH, limits the effects tht the agency can have on the optimal development of universities. We see today assembled as the NIH not a single agency under a Director with broad powers spelled out in the enabling statutes. NIH is indeed fifteen separate budgets put together under selective pressures by different factions and different congressmen. The Director of NIH doesn't control the flow of money from these different spouts. It is regulated by each of the Institutes and Divisions, most of them dedicated to a particular set of diseases. When I was Director of NIH, I would sometimes wake up in the morning and wish that I could say, on striding into the office, "Show me Stanford." I sometimes wanted to know what this whole great constellation of federal support was doing for and to that institution. That was, and I believe still is, impossible. That's one aspect that I find much more pleasantly manageable at Howard Hughes Medical Institute.

Hughes Institute's Complementary Role

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SS: I wanted to ask you about your Institute. It's obviously going to be increasingly important.

DSF: Hughes is very institution-oriented. We choose excellent people. But we also try to consider them and their scientific activities in relation to the whole of science and medicine in the institution. Today research is more a question of teams, of enhancement of one person's activity by what technology and other science surrounds him. Many of the institutions are finding it very difficult to leap into the new paradigms of molecular biology — in terms of instruments, laboratory space or organization — so that they can optimally contend with the change in scientific approaches.

On the other hand NIH has brought up many of the "traditional" NIHsupported scientists to be highly suspicious of the institutional approach. the habit of central determination of who works and who does not, in the academic lab, is a strong one. As we reach further "turns of the wheel" in the biological revolution, however, there will be increasing pressure for "group support" in the places where science is done. Obsolescence or fall in productivity threaten when a necessary team approach cannot be facilitated.

SS: You see your role then at the Hughes Institute as being complementary but also corrective in certain ways?

DSF: Corrective in the sense that there constantly needs to be some push toward reunification of medical schools and their parent universities. The same is so for the need to bring about conjunction of biomedical research in centers where there is no medical school or even a hospital with that in the academic medical centers. Such movement toward reunification also is driven before a flood of new capacities in physics and chemistry or information processing that are constantly merging with biology. The technological enrichment downstream of this confluence gives medical research little repose. Somebody might argue that you also need to get ethics, philosophy, and a lot of other humanities closer to the medical schools again too.

SS: Who, then, are the initiators of programs within the universities and medical schools that come to you and say, "We need the kind of help that you can offer." Is it the clinical faculty? Is it the dean of the medical school? The President of the university?

DSF: All of them come, sometimes bringing important trustees or the governor of the state. Sometimes the source too has to exert some influence on getting different groups among the faculty or the faculty and the administration together. There are few deans who will come and say, "I want to unite this faculty here with that over there." Campus administrators have long been in thrall to get people to sit down and talk about the relationship of the disciplines and what the whole institution most needs -- in new structure, in major instrumentation, in new groups of scientists. We are sometimes able to provide capital, form partnership arrangements, overcome the inertia to change, and help realize some of those needs and unfulfilled ambitions.

Scientific Advances, Educational Challenges

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SS: How does all of this relate to the quality and scope of medical education today? You are focusing on the scientific aspects, but what about the teaching and learning aspects?

DSF: Translating the new biology into practicality must follow discovery. A major effort has to be made to keep people in the faculties who can bridge the gap between lab and bedside -- physicians capable of instilling into students the essential humaneness and enabling them to effectively handle all these new capabilities rising from the sciences. Today few physicians find it possible to be both an excellent clinician and great molecular biologist. But we have to find ways to protect those of the species who try to approach the ideal.

SS: As I ask this question I am thinking about the pushes and pulls with respect to the kinds of doctors and numbers of doctors we needed over the past decade. At one point we needed a great many more; then we thought we might have a glutton, so we focused on the problem of uneven distribution; and now there is some sentiment saying that we still don't have enough or the right kind of doctors. In all of this I take it that the body of those medical students and physicians who are well grounded in the sciences also get pushed and pulled to a degree.

DSF: You may remember that the NIH once had responsibilities for both health manpower and the regional medical programs. This was fortunately before my directorship. The tensions between these problems was too great and NIH proved incapable of making the stretch. NIH has to concentrate on the creation of the scientific members of the faculties of medicine. In this area there are never enough capable people available. Every good school has open chairs. A very common example is in infectious disease.

The medical research establishment has never taken more than 2-5% of the medical graduates. I think there's no alarming lack of available talent. Over the last twenty years the medical schools have had the pick of the graduate students. The losses to investment banking, arbitrage or commerce don't reduce the kinds of minds or temperaments best suited for medical science.

Medical Information and Practice

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SS: Then you've answered one part of my question, but the other part is this: does the aggregate effect of a stable, lively biomedical science component in medical education broadly affect the quality and capacity of physicians?

DF: Unquestionably. The practice of medicine is changing constantly. There have to be those who show the way, who can convey that what is taught today will be obsolete tomorrow. The greatest challenge of today's biological science is how to keep up with it and how to use it.

SS: Fifty years ago there might have been a dozen people working on Rocky Mountain Spotted Fever, and if you wanted to know what was happening on that front you could contact several people and find out. I assume that is not true today with respect to whatever disease might be one's focus. How well are communication systems and information networks keeping up with scientific advances?

DF: It is not without struggle, but they are keeping up. The National Library of Medicine has performed a great service in helping to create and maintain on-line access to the flood of information. So are other agencies. For example, Hughes is active today in concert with the NLM in maintaining a map of the human genome as it emerges from the scientific literature. Part of the system is linkage with other banks of data on inborn errors (McKusick at Hopkins and other clinics) and with the mouse geneticists at Bar Harbor, and the worldwide Human Genome Workshops, so that the editing is up to date. The idea of course is that in creating the "gene dictionary", someday the pediatrician in, say, Omaha, who has a child patient with a C-8 or C-14 translocation, will be able to look it up and be reminded that for him and his patient a run of infectious mono in the school system may be more than routine. The electronic data handling revolution has coincided nicely with the biological one.

SS: It might be even easier to keep up now — the mails were pretty slow fifty years ago, and telephones might not have reached places like western Montana as easily or quickly as they do now.

DF: That's right. At the rate we're going, soon everybody will have his own personal computer and modem and get information a lot more easily than ever before.

SS: How would you characterize the challenge of biomedical science for the next couple of decades? Where are the gaps, what needs doing? Is it just a matter of keeping up with new knowledge and applying it? What is the biggest challenge? It sounds like American medical research is in good shape.

DF: We are in pretty good shape. We have reassuring levels of ignorance to work on, guaranteeing a lifetime of opportunities even for the youngest of us. The key word is "opportunity" -- for continued discovery, for resynthesis of atomized knowledge as it accumulates, for clearer understanding of the nature of life and human potential. I remember how we used to say to each other in the 1960s something like "these are the golden years." The new molecular vision makes the past seem pale. Our greatest challenge is resynthesis, to constantly convert chaotic output of new information into ordered systems that help us understand the whole man and his condition in the whole world. Best, to help us understand ourselves. SS: To return to something you said before, are we not going to run out of physician-scientists who can do what you just said?

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DSF: The pressures continue to build on the physician-scientist who wants to study the whole man. There has been a decline in the number of doctors that do that. The new paradigms for discovery have moved out of reach of the general physician. The molecular biologists today seem to have all the fun.

I'm convinced, however, that cloning all the genes and fitting them with promoters or suppressors, or making monoclonal antibodies will grow boring, unless these wonderful techniques are applied to problems having more and more relevance to man. Good scientists are invariably impatient. They want to turn what they've learned into something of general importance or usefulness. I don't know any kind of good scientist who isn't interested in extending some observation into a useful generalization.

SS: This new situation that you describe -- our attainment of that level of understanding -- is much accelerated by the existance of and activities of the National Institutes of Health. There's no question about that, is there?

DSF: None. NIH is a fountainhead. I've sometimes criticized the way it's structured and the way budgeting decisions are made. But we wouldn't

SS: This is fine, Don. Thank you so much for your time.

CURRICULUM VITAE

Name: Donald S. Fredrickson

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Home Address: 6615 Bradley Boulevard, Bethesda, Maryland 20817

Date and Place of Birth: August 8, 1924, Canon City, Colorado

<u>Family</u>: Henriette Priscilla Dorothea Eekhof Fredrickson Two children: Eric H. and Rurik C.

Education: University of Colorado, 1942-43 B.S., University of Michigan, 1946 M.D., University of Michigan, 1949 Certified: American Board of Internal Medicine, 1957

Chronology of Employment:

1949-1950	House Officer, Peter Bent Brigham Hospital, Boston
1950-1951	James Jackson Cabot Research Fellow in Medicine, Harward Medical School Boston
1950-1952	Assistant in Medicine, Peter Bent Brigham Hospital, Boston
1952-1953	Research Fellow in Medicine, Massachusetts General Hospital, Boston
1953-1955	Clinical Associate, National Heart Institute, National Institutes of Health, Bethesda
1955-1961	Member, Senior Research Staff, Laboratory of Cellular Physiology and Metabolism, National Heart Institute
1961-1966	Clinical Director, National Heart Institute
1962-1966	Head, Section on Molecular Diseases, Laboratory of Metabolism, National Heart Institute
1966-1968	Director, National Heart Institute
1966-1974	Chief, Molecular Disease Branch, National Heart and Lung Institute
1969-1974	Director of Intramural Research, National Heart and Lung Institute
1974-1975	President, Institute of Medicine, National Academy of Sciences, Washington, D.C.
1975-1981	Director, National Institutes of Health, Bethesda
1981-1983	Scholar-in-Residence, National Academy of Sciences, Washington, D.C.
1983-1984	Vice President, Howard Hughes Medical Institute
1984-	President and Chief Executive Officer and Member of the Board of Trustees, Howard Hughes Medical Institute

Present Academic Appointments:

Visiting Scholar, National Library of Medicine, Bethesda, Maryland

Research Interests:

Lipoproteins, lipid transport and metabolism; medical genetics; biotechnology, academic and industrial; science and public policy; medical and scientific institutions and education.

Member:

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Alpha Omega Alpha American Academy of Arts and Sciences American Association for the Advancement of Science American College of Cardiology, Fellow American College of Physicians, Fellow American Federation for Clinical Research American Heart Association, Council for the Study of Arteriosclerosis American Philosophical Society American Physiological Society American Society for Clinical Investigation American Society of Human Genetics Association of American Physicians British Cardiac Society (Corresponding Member) College of Medicine of Valencia (Honorary) Deutsche Gesellschaft fur Innere Medizine (Corresponding Member) Harvey Society (Honorary) Institute of Medicine, National Academy of Sciences Institute of Society, Ethics, and the Life Sciences (Associate Member) International Society of Cardiology Medical Society of Sweden (Honorary) National Academy of Sciences Peripatetic Club Phi Beta Kappa Phi Kappa Phi Royal Academy of the Kingdom of Morocco Royal College of Physicians, London (Fellow) Society of Pediatric Research

Related Professional Activities:

Present

Chairman, National Advisory Committee, NIH Centennial. Member, Advisory Committee, Commonwealth Fund Book Program Member, Board of Directors, Avon Products Inc. Member, Delegation for Basic Biomedical Research Member, Founding Board, Life Sciences Research Foundation Member, Research Advisory Board, E.I. du Pont de Nemours & Co. Member, White House Science Council Member, Charles A. Dana Foundation Awards Panel Member, General Motors Cancer Research Foundation Awards Assembly Member, Metropolitan Life Foundation Medical Research Awards Committee

Related Professional Activities:

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Chairman, Advisory Committee, Minority Faculty Development Program, The Robert Wood Johnson Foundation

Chairman, Committee on Medicine, Federal Coordinating Council for Science, Engineering, and Technology

Chairman, Council on Arteriosclerosis, and Member, Board of

Directors and Central Committee, American Heart Association Member, Council and Executive Committee, National Academy

of Sciences

Chairman, Federal Committee on Research on Biological Effects of Ionizing Radiation

Chairman, Interagency Committee on Recombinant DNA Research Chairman and Member, Medical Board, NIH Clinical Center Lecturer in Preventive Medicine, Georgetown University School of Medicine, Washington, D.C.

Member, Advisory Committee, University of Texas Health Science Center, Houston

Member, Advisory Council on Research, New York State Heart Association

Member, International Science Council, Fondation Cardiologique Princess Liliane, Brussels

Board of Directors, Foundation for Advanced Education in the Sciences

Member, Board of Overseers and the Board of Managers of Memorial Sloan-Kettering Cancer Center

Member, Board of Scientific Advisors, Roche Institute of Molecular Biology

Member, Cardiovascular Research Program Evaluation Committee, Veterans Administration

Member, Cardiovascular Study Section, NIH

Member, Committee on Fats, Food and Nutrition Board

Member, Committee for the Study of Inborn Errors of Metabolism, National Research Council

Member, Council, and Secretary-Treasurer, American Society of Clinical Investigation

Member, Council, Institute of Medicine

Member, Executive Committee, Assembly of Life Sciences, National Research Council

Member, Executive Committee, Section on Atherosclerosis, International Society of Cardiology

Member, External Advisory Committee, Department of Medicine, School of Medicine, University of Alabama, Birmingham

Member, External Advisory Committee, University of Texas Health Science Center, Dallas

<u>Related Professional Activities</u> (continued):

Previous (continued)

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Member, Hazan Prize Committee

Member, Lasker Award Committee

Member, National Academy of Sciences Committee on

Government-University Relationships in Support of Science Member, National Advisory Council for Research, Howard University Member, National Council on Health Care Technology

Member, Nutrition Research Advisory Committee, National Dairy Council

Member, Scientific Advisory Committee, California Biotechnology, Inc.

Member, Scientific Advisory Board, Scripps Research Institute Member, Stouffer Prize Committee

Professorial Lecturer in Medicine, George Washington University School of Medicine, Washington, D.C.

Representative, Governing Board of the National Research Council, National Academy of Sciences

U.S. Coordinator, Problem Area 1, Prevention of Arteriosclerosis, U.S.-U.S.S.R. Cardiovascular Exchange, 1973

Editorial Activities:

Present

Health Affairs, Member of the Advisory Board Editor, The Metabolic Basis of Inherited Disease, Editions I-V

Previous

American Physiology Society, Member and Chairman, Publications Committee; Editorial Boards, American Journal of Medicine, Circulation Research, Journal of Atherosclerosis, Journal of Clinical Investigation, Physiology in Medicine; Editorial and Advisory Board, Journal of Lipid Research

Honors and Other Special Scientific Recognition:

Gold Medal Award, The American College of Cardiology, 1967 The James F. Mitchell International Award for Heart and Vascular Research, 1968

Modern Medicine Distinguished Achievement Award, 1970 The McCollum Award, The American Society for Clinical Nutrition, 1971 Election to the National Academy of Sciences, 1973 Jiminez Diaz Award (Madrid), 1974 Intrascience Award, 1974 La Madonnina Prize for Science (Milan), 1975 Honorary Fellow of the Council on Clinical Cardiology, 1975 The American College of Physicians Award, 1976 Award of Merit, The American Heart Association, 1976 Honorary Doctor of Medicine, Karolinska Institutet, 1977 Purkinje Award (Prague), 1977 Honorary Doctor of Science, University of Michigan, 1977 Irving Cutter Medal (Phi Rho Sigma), 1978 Honorary Doctor of Science, Mount Sinai School of Medicine, 1978 The Gairdner Foundation Annual Award, 1978 Honorary Doctor of Science, University of North Carolina, 1979

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<u>Honors and Other Special Scientific Recognition</u> (continued): Fondazione Lorenzini Medal (Milan), 1980

Election to Fellowship in the Royal College of Physicians and Surgeons, London, 1981

-5-

Honorary Doctor of Science, Georgetown University School of Medicine, 1981

Distinguished Public Service Award, Department of Health and Human Services, 1981

Honorary Doctor of Science, Albert Einstein College of Medicine, Yeshiva University, 1981

The Sarah L. Poiley Memorial Award, New York Academy of Sciences, 1981 Honorary Doctor of Science, University of Medicine and Dentistry of New Jersey, 1982

Distinguished Contribution to Research Administration Award, Society of Research Administrators, 1982

Distinguished Service Award, American College of Cardiology, 1983 Distinguished Service Award, Miami Winter Symposium, 1985 Honorary Doctor of Medical Science, Medical University of South

Carolina, 1985 Honorary Doctor of Science, George Washington University, 1985 The Award for Service to Science, Arthur M. Sackler Foundation, 1986 Honorary Doctor of Science, University of Rochester, 1986.

<u>Honorary Lectureships</u> (partial listing):

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American Swiss Foundation for Scientific Exchange University

Lectures (Basel, Bern, Lausanne, Geneva, Zurich), 1964 John Kent Lewis Memorial Lecture (Stanford), 1967

Seventeenth Annual Convocation Lecture (American College of Cardiology), 1968

Third Bernard H. Pastor Memorial Lecture (University of Pennsylvania), 1968

Marcus R. Caro Memorial Lecture (American Academy of Dermatology), 1968

The Carl Herzog Guest Lecturer (American Dermatological Association, Inc.), 1969

The Distinguished Lecture (Association of American Physicians), 1969 Plenary Lecture, Deutsch Gesellschaft fur Klinische Chemie (Bonn), 1970 St. Cyres Lecture (National Heart Hospital, London), 1970

Wall Memorial Lecture (Children's Hospital of the District of Columbia), 1971

Cardiac Society of Australia and New Zealand and National Heart Foundation Lecturer, 1971

Alpha Omega Alpha Lecture and Visiting Professorship (Johns Hopkins Medical School), 1972

Ernest William Goodpasture Lecture (Vanderbilt), 1972 John C. Higgins Memorial Lecture (University of Oregon), 1972 Harvey Lecture, 1973 Samuel Ballet Memorial Lecture (Philadelphia), 1973 The Jiminez Diaz Lecture (Madrid), 1974 Columbia University Bicentennial Lecture, 1976 Alpha Omega Alpha Lecture (Mount Sinai School of Medicine), 1976 G. Lyman Duff Memorial Lecture (American Heart Association), 1976 Wilson Day Address (University of Rochester), 1977 Irving S. Cutter Lecture (Phi Rho Sigma), 1978

Convocation Lecture (Mount Sinai School of Medicine), 1978

Honorary Lectureships (partial listing) continued:

Wendell Scott Lecture (Washington University, St. Louis), 1978 Convocation Lecture (University of North Carolina), 1979 Geronimo Forteza Lecture (Valencia), 1979

Geronimo Forceza Leccure (Varencia), 1979

Eugene A. Stead, Jr. Lecture (Duke University), 1980 Fiftieth Anniversary Lecture (British Research Society, London), 1980 Public Affairs Address, AFCR/ASCI/AAP (San Francisco), 1981 Commencement Address, Georgetown University Medical School, 1981 Commencement Address, University of Texas Medical Center

(Houston), 1981

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Public Lecture, American Association for the Advancement of Science, Annual Meeting (Washington, D.C.), 1982

Alpha Omega Alpha Lecture (Baylor University School of Medicine), 1982 William Potter Lecture, Thomas Jefferson University

(Philadelphia), 1982

Lilly Lecture, Royal College of Physicians (London/Leicester), 1982 Thorn Lecture, Peter Bent Brigham Hospital (Boston), 1982 Commencement Address, Cornell University Medical School, 1982 Presidential Lecture, Rice University, 1983 Commencement Address, Mayo Medical School, 1983 Anniversary Lecture, Cardiovascular Research Institute, University of

California at San Francisco, 1983 First Likoff-AOA Lecture, Hahnemann Medical School, 1984 Lewis Connor Memorial Lecture, American Heart Association, 1984 Commencement Address, The George Washington University, 1985 Albert Einstein Lecture, New York Academy of Sciences, 1985 75th Anniversary Lecture, The Rockefeller University Hospital, 1985 Faculty Assembly Speaker, University of Texas Southwestern Medical School, 1986

Anniversary Lecture, Harvard Medical School, 1986

November, 1986

DONALD S. FREDRICKSON

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Dr. Fredrickson was born August 8, 1924, in Canon City, Colorado. He attended briefly the University of Colorado, and obtained from the University of Michigan the degrees of Bachelor of Science in 1946 and Medicine in 1949. Upon graduation he went to Boston for ward and laboratory training in clinical medicine and research at the Peter Bent Brigham Hospital, the Massachusetts General Hospital, and Harvard Medical School. In 1953, he moved to the National Heart Institute, Bethesda, Maryland, as one of the first class of clinical associates to open the Clinical Center at the National Institutes of Health. He remained at the National Heart Institute from 1953 to 1974, during which time he was a staff scientist, later, a section head, and then chief of the Molecular Disease Branch. While simultaneously maintaining his research, Dr. Fredrickson also served as Clinical Director (1961-1966), then Director (1966-1968) and finally Director of the Division of Intramural Research (1968-1974) of the Heart Institute.

Throughout his career, Fredrickson's scientific interests have been concentrated upon the metabolism of fats and their transport in the bloodstream, a subject of special importance in relation to arteriosclerosis. His work combined clinical investigation and fundamental laboratory studies of the structure and function of the plasma lipoproteins. In Fredrickson's laboratories were discovered several of the dozen known apolipoproteins that enable cholesterol and other lipids to be carried in the bloodstream. A new classification was developed of disorders in which concentrations of blood cholesterol or other fats carried in lipoproteins are abnormally elevated. Adopted by the World Health Organization the system is still in use around the world today. It has been of value in ordering a once chaotic area of medical knowledge that is still undergoing rapid revision and expansion. Much of Fredrickson's career has also been concerned with genetics and five new inheritable diseases of lipid metabolism were recognized in his laboratory, including Tangier disease, given its name for the island in the Chesapeake Bay from which came the first patients. Fredrickson is a founding editor and author of "The Metabolic Basis of Inherited Disease", one of the classical books of its genre and now being prepared in its sixth edition since 1960.

In July 1974, "hearkening to the beat of other drums," Dr. Fredrickson left NIH to become the second President of the Institute of Medicine, National Academy of Sciences. After one year, however, he accepted the invitation of President Ford to fill the vacant chair of the Director of NIH. He held that position from July 1975 during the term of President Carter and the first part of the Reagan administration, serving serially under Secretarys Weinberger, Matthews, Califano, Harris and Schweicker. Fredrickson was the eleventh director of the NIH in its nearly one hundred years of existence. As he assumed command, the years of great expansion, presided over by James A. Shannon under the Congressional patronage of Senator Lister Hill and Congressman John R. Fogarty, were coming to an end. The chief concerns of the NIH turned to stabilization of the support of academic research and responsibilities which had now broadened to include a number of social issues from cost-benefit analysis and technology assessment to ethics of research and control of technologies emerging from the "new biology" for which NIH-supported research had been preeminently responsible. Among the changes in the roles of the NIH director was a great increase in interaction with the legislature. During the 94th Congress alone, Fredrickson testified more than thirty times.

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As the head of the agency which is the world's largest supporter and conductor of biomedical research, Fredrickson became deeply involved in a number of issues related to the organization, financing, and public governance of science. Doubtless the single most dramatic of these occurred between 1975 to 1978 at the height of controversy over the use of powerful new techniques for genetic engineering. His became the responsibility for establishment and direction of a voluntary system for the regulation of recombinant DNA research in the United States from 1976 to the present. He chaired the Federal Interagency Committee on Recombinant DNA Research from its establishment in 1976 to 1981.

As NIH Director Fredrickson developed new techniques for the planning and budgeting of research by NIH. The most significant aspect of this was the procurement of an agreement between the Congress and Executive Branch to make the capacity to support investigator-initiated research grants the cornerstone for setting the annual NIH budget. The "basic science stabilization" goal awarding a minimum number of research grants each year (the first goal was a 'floor' of 5,000 grants) became and continues to be a rallying point for debate during the annual process of determining the levels of federal science support. Dr. Fredrickson established the Technical Consensus exercises which now are a regular feature of research assessment at NIH and abroad. He also was a founder of the National Toxicology Program.

After resigning from NIH for the second time in July, 1981, Fredrickson then spent eighteen months as Distinguished Scholar in Residence at the National Academy of Sciences in Washington. As a member of both the White House Science Council and the Academy's Ad Hoc Committee on Government-University Relationships in the Support of Science, he was afforded an exceptional opportunity to study first-hand the government support of all the sciences in both the academic and federal laboratories. Fredrickson left the Academy in February, 1983 to serve as a consultant, and then as a Vice President of the Howard Hughes Medical Institute. In 1984 he was appointed to the Board of Trustees of the Institute and elected President and CEO. HHMI is a non-profit medical research organization which was founded by the aviator-industrialist Howard R. Hughes. It has operated research laboratories in close affiliation with academic hospitals and medical centers across the country since 1953. Until recently the Institute was the sole owner of the stock of Hughes Aircraft Company. Upon the sale of this defense electronic company to General Motors in December 1985, the endowment of HHMI became slightly more than \$5 billion. Fredrickson could thus be said to have exchanged the direction of the world's largest public conductor of biomedical research for that of the largest single private one.

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His major challenges now are to lead the establishment of the philosophy and structure of a greatly expanded organization with a unique opportunity for positive influence on the biomedical sciences, a field in which he has spent his entire career. The Institute has recently announced a goal of expending at least a billion dollars over the next five years in its laboratory and training programs that presently emphasize molecular genetics, the neurosciences, immunology, various aspects of cell and structural biology and metabolism.

Fredrickson is a member of numerous organizations including the National Academy of Sciences, the American Academy of Arts and Sciences, and the American Philosophical Society. He has received a number of honorary degrees and other honors.

Dr. Fredrickson was married in 1950 to Henriette Priscilla Dorothea Eekhof of The Hague and then a law student at Leyden. They have two sons, Eric and Rurik. All are fluent in Dutch, avid skiers and passable tennis players.