

NIH, ALMA MATER

I RECENTLY ATTENDED the first National Institutes of Health (NIH) Alumni Reunion in Bethesda. For me, and undoubtedly for others, it was the first alumni reunion of any kind. Perhaps we were all rather reluctant to repeat the experience of the college graduate who returned home from a class reunion in a very depressed mood. "My classmates" he told his wife, "have all gotten so fat and bald they didn't even recognize me."

We did not gather from distant places primarily for good fellowship, although we found that the warmth and devotion of our NIH friends would have been worth the trip. Rather we came together because the NIH, more than any college or university, shaped our scientific lives in the most profound way. The NIH is an institution of such unique quality, and of such importance for the training of future generations of scientists and for the health and welfare of our society, that we must do everything possible to preserve its vigor.

Institutions and nations come and they go. In worrying about the longevity of the NIH we should know something of its origins and history. It will help us assess its physiological age and anticipate the problems that might cloud its future.

The NIH started in 1887 in a small room at the Public Health Service Marine Hospital in Staten Island. It was a laboratory in which to practice the new science of bacteriology. Four years later, in enlarged quarters in Washington, it was called the Hygienic Laboratory. Joseph Kinyoun, the first chief of the laboratory, was sent for training under Robert Koch in Berlin and to the Pasteur Institute in Paris.

In 1901, the Congress provided for a new and still larger laboratory at 25th and E Streets to investigate infectious and contagious diseases and other matters pertaining to the public health. Some Public Health Service (PHS) officers were detailed from time to time to the laboratory in order to become familiar with bacteriologic diagnosis of contagious diseases and to investigate their causes and prevention.

Original and important investigations of epidemic diseases such as cholera, plague, and yellow fever were made at the Hygienic Laboratory.

One of my favorite microbe hunters of this era was Joseph Goldberger. He came to this country from Europe in 1881 at the age of seven. He grew up in New York's Lower East Side in poverty. Yet he managed to go to City College and get medical training at Bellevue Hospital Medical College, now New York University Medical School. He joined the PHS in 1899, not for money but for adventure. For the next ten years, he made important contributions to the understanding and control of several infectious diseases including yellow

fever and dengue fever, each of which nearly killed him.

In 1914 he was sent to the South to find the organism of pellagra. Each year epidemics of this disease afflicted hundreds of thousands of people with skin lesions, weakness, diarrhea and mental derangements. Many were committed to asylums. The economic effect of the disease was widespread on the cotton plantations where the workers were afflicted.

Goldberger observed that in institutions with severe epidemics, inmates were affected, but the staff people were not. This was a remarkable disparity for a con-

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tagious disease. He noted, too, that whereas inmates ate corn bread, grits, molasses, and fat back, the staff ate meat, milk, and vegetables. When he fed the inmates' diet to dogs, they developed blacktongue, the canine analogue of pellagra. When he fed them meat, milk and vegetables, they were cured. People fed a good diet were miraculously cured; and hopelessly insane people were discharged from asylums.

Goldberger proved by controlled experiments that pellagra is a dietary deficiency disease. This landmark discovery of a nutritional deficiency led him to intensive assays of foods for their anti-pellagra value. Nutritional research was a novel departure for the Hygienic Laboratory, which had been oriented to infectious diseases. Unfortunately, Goldberger died in 1929, eight years before nicotinic acid was identified as the anti-pellagra vitamin.

During World War I, the Laboratory supported basic studies in physiological chemistry, such as those of Baird Hastings, who attended the reunion.

The name of the Hygienic Laboratory was changed to the National Institute of Health in 1930. Nevertheless, I would date the modern history of the NIH from 1938. This was the year that signalled a major increase in size and scope. In that year the NIH moved into six red brick buildings of Georgian design, built in Bethesda on a 90-acre estate donated by Mr. and Mrs. Luke Wilson. Eventually, the campus swelled to over 300

acres and 50 buildings housing 12,000 staff. Beyond growth in size, the move to Bethesda also led to a broadening of research directions, most notably creation of the National Cancer Institute.

I find it hard to believe that my own acquaintance with the NIH goes back almost that far. [If I include some personal narrative, it is because I believe that my experiences at the NIH were reasonably typical of its many hundreds or even thousands of alumni, who, over time, have formed the essence of the institution.]

I came to the NIH in the fall of 1942 as a commissioned PHS officer. I had been transferred from sea duty at the suggestion of a ship captain exasperated by my inattention to naval etiquette. I was assigned to work on rat nutrition in a section directed by William H. Sebrell. He had succeeded Joseph Goldberger and had been trained by him; so had some of the laboratory aides who prepared the synthetic animal diets we used. I had intended to practice medicine. But after a year, I found full-time laboratory investigation even more challenging and exciting. Thomas Parran, who was then Surgeon-General, told a group of us that he wanted PHS officers not so well-rounded but sharper at the edges. So an assignment to the NIH might be more than a two-year rotation.

Rat nutrition and a search for the vitamin, folic acid, were interesting until I saw greener pastures. I was enthralled by a seminar in which Edward Tatum presented the one gene-one enzyme concept based on his neurospora work with George Beadle. Seminars were held then in the quaint room of a rustic cottage, called Top Cottage, later moved by the Clinical Center and erased by Building 31. An even greater revelation for me was the enzyme work of Fritz Lipmann, Herman Kalckar, Carl Cori and Severo Ochoa. Here was a window on another world of science: enzymes of astonishing specificity and catalytic potency linked the combustion of foodstuffs to the generation of ATP which made the cell grow and the muscle move. What fantastic natural poetry! But there was no one at the NIH doing such enzymology or biochemistry.

I will be forever grateful to the NIH for sponsoring me as a PHS officer to train with Severo Ochoa in New York in 1946 and then with Carl Cori in St. Louis in 1947. I was convinced that the vitamin hunters had exhausted their prey, as had the microbe hunters a generation before them, and that the next era would belong to the enzyme hunters.

The NIH to which I returned in 1947 had not changed much in the war years, but seeds had been planted and were beginning to sprout. The next year an S was added after Institute on the lettering of the Building 1 architrave, signifying the creation of Dental, Heart, and other categorical institutes. The Research Grants Division was established. Planning for the Clinical Center was started.

I regard the five years between 1947 and 1952, during which I worked at the NIH, as the most productive and gratifying in my scientific life. I recall a visit in 1950 from Gerty Cori. She lamented my being in a

government laboratory. How could I convince her that with my close colleagues Bernard Horecker, Leon Hoppel and Herbert Tabor I was enjoying an ideal academic environment.

When I moved in 1953 to be a professor and chairman of a department in a medical school, I made two errors in judgment. I believed that the advent of the Clinical Center and the disease-oriented institutes would stifle basic research at the NIH. And, I believed that administrative life in a university would be unobtrusive. As we all know, research at the NIH flourished, and I learned that university administration can indeed be burdensome.

The greatness of the NIH rests on achievements in three areas: first, research at the NIH, second, guidance of the extramural grants and training programs, and third, training of scientists at the NIH. Each has been successful beyond my most optimistic expectations.

As for research achievements: first, in the past 25 years, no single institution has so dominated the journals of basic medical science, and some of these contributions have been of stellar magnitude. I could easily use the rest of this essay to recite them.

Second, the extramural grants and training programs have been the single most important foundation for the biological revolution of the postwar period. Let me expand on this.

Guided initially by NIH scientists, the peer review system for awarding grants and fellowships has administered tens of billions of dollars with a scrupulous regard for quality and without a hint of chicanery. I know of no government program of this magnitude with such a magnificent record.

The results of the massive support of biomedical science training and research during the past 20 years have been extraordinary. No one imagined that we would acquire so quickly the firm grasp we have today of the basic designs of cellular chemistry and its regulation. The nature of heredity, clouded in formal genetic language only 20 years ago, can now be described in explicit chemical terms. If the first half of this century belonged to physics and chemistry, then the second half belongs to biology.

Knowledge of the structure of genetic material and the way in which cells regulate their expression promises great benefits in medicine and agriculture. Vigorously applied, this new knowledge could transform the image of health and disease as drastically as any advance in history. Beyond these practical benefits, the new knowledge of gene and cellular structure gives us deep esthetic pleasure. We have new insights into the origin of life on earth and a basic appreciation of how man is related to his earthly ancestors and neighbors.

I have cited two facets of the NIH: intramural research and the extramural support programs. The third facet, the training of scientists at the NIH, is less recognized but of equal rank with the other two. In the untrammelled atmosphere of well-equipped, well-directed laboratories, hundreds upon hundreds of young M.D.s

and Ph.D.s were introduced to professional science. Some remained at the NIH. But the majority left to staff research, clinical, and administrative departments throughout the world. Today they populate and, as professors, chairmen, and deans, direct the finest university departments of basic medical science and clinical science. Today they are the clinicians in the leading hospitals. Today they are the research directors of the foremost pharmaceutical companies. They bring a novel outlook from their training in basic biological and chemical sciences to the lecture hall, laboratory, bedside, and to industry. The NIH is truly a National *University of Health*.

I am not now part of the NIH nor do I have sentimental attachments to institutions. I therefore can state with minimal bias that the NIH has been and is today an integral part of the machinery of basic and applied research in the country, and so it must remain. The NIH is absolutely essential for the future health and well being of our nation and all of mankind.

Why then was there an NIH Alumni Reunion? The alumni gathered, not only to recall the past and present achievements of the NIH, but to express their concern for its future. Despite its superb record, and its dedication to science and conquest of human disease, the NIH is being subjected to severe criticism. Unfortunately, the NIH has grown to a size that makes it vulnerable, although much of this growth was due to public health programs imposed upon it. The enlarged budget is an obvious target for budget cutting and for anti-science forces. As with all worthwhile things the struggle for survival is never won. This is even more true for support of science than for other institutions in society. Let me explain by contrasting the nature of science progress with the support of science by society.

The goals and attitudes in research have not changed in any fundamental way for hundreds of years. Achievement in science depends on the same human qualities required in other professions, in art, and in business. We find among scientists the same variety of abilities and styles, of strengths and weaknesses, that are found among lawyers, doctors, politicians and businessmen. What is different is science itself. Science differs from other human activities in the way it is practiced and the way it progresses. The pattern of science is a stepwise extension of what was done before.

The steps are small and usually do not follow a path or seek a goal. Rather they develop as in Walpole's story of three princes of Serendip, who in their travels were always discovering by chance or by sagacity things they did not seek.

Whether serendipitous or planned, scientific activity, seen with perspective, always moves forward. Science is thus unique among human endeavors in the polarity of its movements. We call it progress. I must repeat that it is science that is extraordinary, not the scientist. Because science enables ordinary people to express their creative talents in a purposeful way, their humble probings, picayune individually, combine to exert

irresistible forces in exposing the grand designs of nature.

The flow of science to me resembles the movement of rivers. Rivers have a fixed direction and continuity as they flow down to the sea. Like rivers, the pace and dimensions of scientific movement vary enormously. But shallow or deep, broad or narrow, sluggish or swift, the movement is inexorably forward.

There may be eddies in sciences as in rivers; and there may even be apparent reversals of direction. In recent memory, Profim Lysenko and his followers in the Soviet Union stifled genetics and molecular biology there for a whole generation, and Soviet medical science and agriculture still carry the deep scars of that period.

In contrast to the forward movement of science, the support of science by society has no direction. The attitude of society toward its social problems has been likened to the swing of the pendulum. And so also the support of science, rising and falling as it has throughout history, does not resemble a river, but rather the movement of tides.

In the support of NIH and science in this country, we saw a very low tide during the 1930s, before the War. Then there followed a strong high tide for twenty years after the War. For the past ten years, the support of science has been visibly ebbing away. Funds for basic research by excellent scientists at the NIH and elsewhere have been cut at a time when inflation and advanced technology call for increases. And the support for the training of our best young scientists has been drastically curtailed. This support for research and training cannot be finely regulated. When the flow of science support is turned down, the stream of progress dries up and cannot be restored for years. Why are we reversing the tide of science support?

It cannot be for reasons of sound economy. We invest in medical research only about 3% of the gross product of a 100 billion dollar health industry. There is no industry based on technology today that spends less than 5% of its product on research and development.

The lifeline of medicine has been and will remain science and technology. When medicine grapples with the unknown, the art of witchcraft eventually supervenes. In the future, medicine must become more reliant on science and technology, not less so.

The difficulty with research support in our society, I have come to realize, is the failure to understand the nature and importance of basic research. This is true of the lay public and physicians, of legislators and political leaders. They do not realize the long time scale of basic research, and that its utility, its applicability, is not obvious. If it were, it would be developmental rather than basic research. They do not realize the quantitative scale of basic research, the need for a critical mass of research effort. Fragments of knowledge unwelcomed and unexploited are lost as were Gregor Mendel's basic genetic discoveries. They also do not

realize that the scientists who do basic research are the least articulate, least organized and least able to justify what they are doing, and this is in a society where selling is so important, where the medium is the message.

If there were a record of research grants in the Stone Age, I believe it would show that the major grants were awarded for proposals to build better stone axes and that the critics of the time would have ridiculed a tiny grant to someone fooling around with metals. The record clearly shows that X rays were not developed for their value in medicine and surgery but because physicists were curious about some utterly esoteric questions about electricity in a vacuum. The record also shows that antibiotics were discovered and brought to the point of clinical trial not by pharmacologists searching for therapeutic drugs, but by a bacteriologist and a biochemist who were curious about how enzymes dissolved bacterial walls.

In our more recent experience who among us can forget the scourge of polio? It was basic research in virology, immunology, and cell culture that gave us the polio vaccine. Otherwise we would be spending billions on more elegant iron lungs and on Sister Kenny physiotherapy centers.

In concluding, I want to emphasize the fact that no one person, or committee, planned the extraordinary

development of the NIH today. It is a serendipitous discovery. By chance and sagacity we have an institution of the greatest value for the health of our society. In the Bicentennial Year spirit let us celebrate and preserve it as we do our Constitution. Had we had the good sense to develop national institutes of comparable stature in agriculture and energy resources, many of our present problems would be less serious.

There are two compelling reasons why society must support the NIH and science. One is substantial: the obscure science of yesterday is curing diseases today and will do more tomorrow. The other reason is cultural. The essence of our civilization is to explore and analyze the nature of man and his surroundings. As proclaimed in the Bible in the Book of Proverbs: "Where there is no vision, the people perish."

Despite the current emphasis on food and fuel, America's greatest strength is not in mineral resources, nor in hydroelectric power, fossil fuels, nor in its soil. It is not in the accumulation of a huge weapons arsenal either. America's strength is in the moral and intellectual resources of the people.

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