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NIHAA Update

Scientist, Administrator, Humanist

DeWitt Stetten Dies; Shaped NIH Research for Over Three Decades

Dr. DeWitt Stetten Jr., NIH deputy director for science, emeritus, and senior scientific advisor to the NIH director, died Aug. 28 of congestive heart failure at Fernwood Nursing Center in Bethesda.

Born May 31, 1909, in New York City, Stetten, known affectionately to his friends as "Hans," was the second child of a prominent surgeon. As a boy he attended Horace Mann School, an experimental school associated with Teacher's College of Columbia University. In 1930, he received his A.B. degree magna cum laude from Harvard College and was named a member of Phi Beta Kappa. Although his first love was biochemistry, he was persuaded by his Harvard tutor and mentor, Frank Fremont-Smith, to attend medical school before embarking on a laboratory research career.

*(See **Stetten** p. 30)*

Dr. DeWitt Stetten Jr.

First Human Gene Therapy Trial Debuts at NIH

By Carla Garnett

After more than 3 years awaiting federal approval, the first human gene therapy clinical trial got under way in September at the Clinical Center.

"We feel that gene therapy is potentially a major new therapeutic option that should have significant effects in the next century," announced Dr. W. French Anderson, chief of NHLBI's Molecular Hematology Branch and one of the trial's three principal investigators.

"We also feel that as important as anything else is to get started," he said.

"The possibility of coming up with a therapy that really can fundamentally help is very exciting," echoed Dr. R. Michael Blaese, chief of the cellular immunology section of NCI's Metabolism Branch and another principal investigator.

"Everything is sort of slow steps," he continued. "I think this is a small step as well but it's a very exciting one."

The treatment, historic in its implications but comparatively simple in its procedure, began mid-day Sept. 14 in the pediatric intensive care unit.

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Federal Agencies Ranked

NIH Work Force Rates Tops in Survey

Only national security is nearer and dearer to the hearts of former federal executives than health research and money, say members of the Washington-based Council for Excellence in Government.

NIH tied with the Federal Reserve as the second most respected federal agency, according to 250 former government executives and council members who recently completed a *Fortune* magazine survey.

The National Security Council was rated first. NIH finished ahead of such contenders as the Council on Economic Affairs (fourth), the Office of the Treasury Secretary (fifth) as well as the CIA and the FBI (eighth and ninth).

Almost 90 government agencies were rated on four criteria: quality of management; quality of work force; quality of service; and return on the tax dollar.

Survey respondents, all of whom are now in the private sector, were asked to rank the agencies based on personal experience with the agency or perception of the agency's competence at accomplishing its mission.

"The top-rated agencies are all older, more established agencies for which a political consensus exists about their

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mission," said Mark A. Abramson, council president. "They are generally highly visible, and they all have a reputation for stability of leadership and for seeking and retaining excellent people."

Least respected agencies include the Bureau of Indian Affairs, Small Business Administration, the Indian Health Service, the Department of Education, and the Department of Housing and Urban Development.

The bottom-ranked agencies "have suffered from declining resources and high turnover of staff, often because they are politically controversial," said Abramson. "They tend to be newer organizations whose mission is less clear and for whom there is not a national political consensus about their worth."

The three top-rated agencies—the "superstars"—were all rated first on one or more of the judging criteria. The Federal Reserve was rated tops for quality of management and quality of service; the NSC tops for return on tax dollar; and the NSC and NIH shared the top ranking for quality of work force.

Ranked in the next-to-highest category was NIH's cousin, the Centers for Disease Control.

According to a spokesman, the council did not give overall ratings to large departments whose autonomous units had high name recognition, such as the Department of Health and Human Services. Instead it rated a number of major agencies within the large departments. In the case of HHS, this led to a range of ratings, with "best" for NIH and CDC, "good" for the Food and Drug Administration, "fair" for the Alcohol, Drug Abuse and Mental Health Administration, and "needs improvement" for the Indian Health Service.

Also excluded from the survey were such large central management agencies as the General Services Administration and the Office of Personnel Management; the smallest agencies were similarly unrated.

Highlights of the survey's findings are reported in the Nov. 19 edition of *Fortune*.

NLM Calendar Available Through Friends

A colorful 1991 National Library of Medicine wall calendar—featuring twelve illustrations, mostly drawn from the library's historical collections—is now available from the Friends of the National Library of Medicine, 1527 Wisconsin Ave., N.W., Washington, DC 20007. The price is $10 per calendar ($8 for members of the Friends, staff and alumni of the NIH/NLM). Please add $2 for shipping and handling; if ordering more than one calendar, add an additional $1 per calendar.

"The Alchymist," a 17th century etching from NLM's History of Medicine collection, is one of the illustrations in the 1991 NLM calendar, offered by the Friends of the NLM.

Among the illustrations in the calendar, most of which are in full color, are a 1514 engraving on melancholy by Albrecht Durer, an 1825 etching caricaturing indigestion, an 1887 lithograph of Louis Pasteur, and a 1987 AIDS conference poster. Important anniversary dates in medical history are given for each month, as well as interesting anecdotes and quotations related to the themes represented in the pictures.

NIHAA Update

The NIHAA Update welcomes letters and news from readers. We wish not only to bring alumni news about NIH, but also to serve as a means for reporting information about alumni—their concerns, information on recent appointments, honors, books published and other developments of interest to their colleagues. If you have news about yourself or about other alumni, or comments on and suggestions for the NIHAA Update, please drop a note to the editor. We reserve the right to edit materials.

Editor's Note

The NIHAA Update, is the newsletter of the NIH Alumni Association. The NIHAA office is at 9101 Old Georgetown Rd., Bethesda, MD 20814, (301) 530-0567.

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NIHAA Forum

A Defense of the Human Genome Project

By Dr. James Watson and Dr. Norton Zinder

The following is a reprint of a letter sent to the New York Times *by James D. Watson, director of the human genome project and Norton Zinder, John D. Rockefeller, Jr. Professor, Rockefeller University, and Chairman NIH Program Advisory Committee on the Human Genome.*

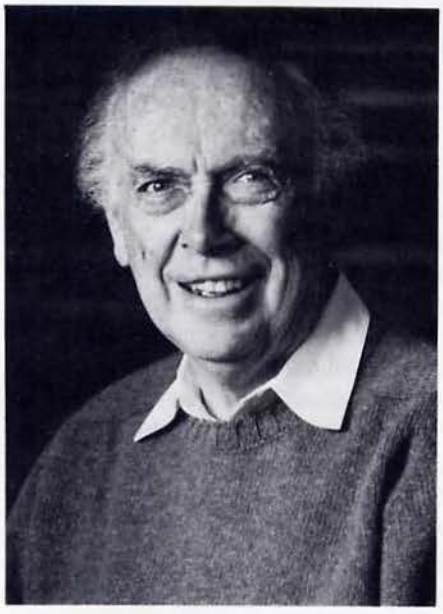
Your paper has recently published opinions critical of so-called "big science," including the Human Genome Project. The project is nothing like the "big science" research and development initiatives with which it is continually compared.

First, the Human Genome Project is not a large piece of hardware located in a single place to be operated by a single group. More than a hundred laboratories in every corner of the continent will participate in the project. Most genome project laboratories will contain about the same number of workers as any typical biomedical research lab.

Second, the Human Genome Project cannot fail. Each step we take en route to our ultimate goals will make it easier for scientists to find genes. Like the system of interstate highways spanning our country, the map of the human genome will be completed stretch by stretch, beginning now.

Our first major goal, to construct a fully connected system of maps of each of the human chromosomes, will guide researchers more quickly and cheaply through the labyrinth of human DNA to the genes they are so eager to find. Biomedical investigation will flow along any part of those pathways as soon as they are complete, well before the entire system is mapped.

Thousands of human diseases have their roots in malfunctioning genes, and many others have strong genetic co-factors. Despite exciting recent successes, tracking down genes is now a very difficult task. Using current chromosome maps, gene hunts are long, arduous, and enormously expensive. Just ask the people who have done it. Discovery of the gene for cystic fibrosis—an "easy" find according to those scientists—took seven years at a very high cost. Sadly and more typically, the eight-year search for the devastating Huntington's



Dr. James D. Watson

disease gene has yet to bring forth the villain, despite the vigorous efforts of a cadre of superb scientists. For diseases resulting from the interactions of more than one gene, discovering the underlying genetic factors will be impossible without a detailed map.

Researchers studying a roundworm have mapped 95 percent of its genome. Such a map has reduced the time it takes to find a gene in that animal from over a year to merely weeks. It is possible today to construct similar maps of human chromosomes. A central goal of the Human Genome Project is to deliver those human maps over the next five years to the research community so scientists can get on with the study of how genes work, in both health and disease.

NIH invests in the search for genes because we believe having a gene in hand is the first step in the characterization of molecular defects that result in disease. Progress in understanding the causes of cancer, for example, has been pushed forward tremendously by the discovery of cancer genes. We must now make deliberate efforts to surmount the next technological hurdles that today keep scientists from understanding the molecular essence of other tragic and devastating illnesses, such as schizophrenia, Alzheimer's disease, alcoholism, and manic depression.

Once genes are found, their alterations and defects are analyzed by DNA sequencing to give us their specific structures. Current technology is still too slow and costly to sequence even the amount of DNA contained in a small piece of one human chromosome. To fulfill its ultimate goal of sequencing the three billion subunits of human DNA, the Human Genome Project must stimulate development of faster and cheaper sequencing technologies. Large-scale sequencing of the human genome is not scheduled to begin until the cost of sequencing is reduced significantly, to less than $1 per subunit.

More efficient sequencing technologies will make laboratory life infinitely easier for the many biomedical researchers longing to know the secrets locked away in a lengthy DNA strand they painstakingly isolated. The ability to sequence DNA quickly and cheaply will also provide the technological

*(See **Genome** p. 4)*

Genome (continued from p. 3)

basis for a new era in the laboratory. The Human Genome Project will greatly accelerate the speed at which important "natural" drugs, such as the already available tissue plasminogen activator, erythropoietin, and interferon become available to patients.

The concept of a Human Genome Project received several rigorous reviews by independent scientific panels. Each of these committees, which contained members initially opposed to the project, concluded that such a project is both feasible and important to the advancement of U.S. science, industry, and public health.

Dr. Norton Zinder

The amount of money we ask to accomplish the task, $200 million a year, is commensurate with the genome project's role in the fight against many serious health problems. The contributions the Human Genome Project will make to the full range of biomedical research the NIH supports make it an economical and worthwhile investment.

Americans have always and proudly dared to envision great things. That is the only way we will accomplish them. The Human Genome Project celebrates not only the wonder of our genetic endowment but also the grandness of the human spirit.

NIH Creates Office of Education, Fordis Named Director

The next decade offers unparalleled opportunity for scientific discovery. Yet in the face of such possibilities, there has been a precipitous decline in the number of young Americans who are training for careers in biomedical research. To address this problem, NIH has created a new Office of Education that is responsible for the development and coordination of a variety of programs and initiatives that will be part of a strategy designed to reverse this trend.

In addition to providing a focal point for postdoctoral recruitment efforts across institute lines, the Office of Education plans to establish a pipeline of opportunities for young people at varying stages of educational development. These opportunities will include, but not be limited to, the Clinical and Research Associates Program, the Clinical Electives and Summer Research Fellowship Programs, and the NIH/ Howard Hughes Medical Institute High School Summer Research Program.

In collaboration with the Educational Commission on Foreign Medical Graduates, the office has developed the NIH/ International Medical Scholars Program, which will permit foreign physicians to come to NIH for training in clinical and basic research.

The office will also assume responsibility for the administration of all NIH continuing medical education programs, as well as the continuing accreditation of graduate medical education programs.

Dr. Michael Fordis, a former NHLBI and NCI researcher, has been named director of the office by Dr. Joseph E. Rall, NIH deputy director for intramural research.

Dr. Michael Fordis

A native of California, Fordis earned his B.S. at the University of California, Irvine; his M.D. at the University of California School of Medicine in San Diego, where he also completed his residency in internal medicine. In 1977, Fordis joined the Hypertension-Endocrine Branch of NHLBI, where he studied the biochemistry of vasoactive peptides. With a growing interest in the regulation of development, he joined the Laboratory of Chemical Biology in 1981 and investigated the developmental expression of human globin genes. Before accepting his current position, he continued his studies in the Laboratory of Molecular Biology, NCI, where his work focused on genes that suppress cellular proliferation.

The office is located in Bldg. 10, Rm. 1C129 and the telephone number is (301) 496-2427.

NIH Research Festivities Offer Something for All

By Anne Barber

"A day just for ourselves," said Dr. Joseph E. Rall, NIH's deputy director for intramural research.

"Like a family reunion," said Dr. Philip S. Chen Jr., NIH's associate director for intramural affairs. "It is a great thing for getting together NIH's intramural program. We are interested in bringing together scientists who now do not have much contact."

Rall and Chen are talking about Research Festival. Begun 4 years ago, it was expanded this year to include an extra day of activities. This year there were 5 symposia, 35 workshops and 383 posters displayed during the 2 days of activities—Sept. 10 and 11.

For the first time, a Distinguished Alumni Award was presented. The recipients were Drs. Emil Frei III and Emil Freireich who developed the first successful cure for childhood cancer using chemotherapy.

NCI's director for the Division of Cancer Treatment, Dr. Bruce Chabner, chairman of the symposium honoring Frei and Freireich, said the idea for having a Distinguished Alumni Award yearly belonged to Dr. Abner Notkins and the NIH Alumni Association. Notkins serves as chairman of the organizing committee for the association.

"NCI had the privilege to bestow the first award," said Chabner, "and we chose two of our most distinguished alumni. They were here 35 years ago and many of us have profited from their research."

"I was one of the last trainees of these two gentlemen during their last years at NIH in 1960," said former NCI director Dr. Vincent DeVita, now of Memorial Sloan-Kettering. "Cancer was considered a killer and chemotherapy was talked about despairingly because of the side effects and tolerance.

Dr. Emil J Freireich (l) and Dr. Emil Frei III were winners of the NIH 1990 Distinguished Alumni Award. In a speech prepared for the presentation, Dr. Samuel Broder, NCI director, characterized them both "as practicing both pure and practical science in the service of saving lives. I see their lives as serving the highest of ends. I see them as a model of the new clinician scientist so necessary to the continual prevention, eradication and control of cancer."

"The main issue of the sixties was whether or not cancer chemotherapy could cure cancer. These two doctors established the dose response and toxic effects to come up with the combinations used here in the fifties. Their aim was curing leukemia. Their idea was controversial but stimulating."

Continued DeVita, "Their model was childhood leukemia. I remember being quite stunned when I saw their first remission from chemotherapy. The general reaction was indignant rejection, opposition, then cautious adoption.

"Frei taught me not to believe anything I was taught unless I saw the proof," he continued. "There is a quote I leave to all trainees. I don't know who said it but the quote is: 'Do not follow where the paths may lead, go instead where there is no path and leave a trail.'"

Dr. E. Donnall Thomas of the Fred Hutchinson Cancer Center and a member of its marrow transplant team stated that in the 1950's there was no corrective therapy for leukemia. "The first bone marrow paper was published in 1957 and transplantation followed in 1959. Now platelet transfusions have become routine." Thomas recently shared the 1990 Nobel Prize for Medicine or Physiology.

Freireich, presently at the M.D. Anderson Cancer Center, said in his acceptance speech, "I spent 10 years at the Clinical Center and the things we (Frei included) learned there have guided us through the past 25 years.

"We were bold enough to propose a cure. It proved to be rational and I was lucky I got to see this proven during the past 25 years. Normally, the problem in this field is that we don't live long

*(See **Festival** p. 6)*

Festival *(continued from p. 5)*
enough to see what the long-term results are.

"Now we have to work with genetics. Cellular genetics is just overpowering and molecular genetics is now exploding. I believe the next 25 years will be more exciting and I hope I'll be here to talk about them," Freireich concluded.

When Frei arrived at the Clinical Center in 1955, his goal was research. "We did new things with the idea that we did not bring patients into the Clinical Center to treat them in routine fashion," he said.

"We had new techniques, we developed novel approaches from basic and clinical sciences. Today, we combine both novel and traditional approaches.

"We need to give the investigator resources and a chance to go with his ideas," Frei continued. "We need to have primary goals relating to cancer research and the freedom and resources to reach them. This is what should be done at a place like the National Institutes of Health."

Rall, who gave the opening remarks at the AIDS symposium later the same day, received a photograph of the NIH campus in honor of his 70th birthday being celebrated this year. Dr. John Gallin, chairman of the Research Festival '90 organizing committee and director of NIAID's Division of Intramural Research, presented the framed photograph. "In keeping with the spirit of the festival, we are honoring someone who has been at NIH for more than 35 years and helped us establish this Research Day." The plaque was signed by laboratory chiefs and directors.

Dr. Samuel Broder, director of NCI, emphasized how important it is that NIH have a research festival for the intramural program. "It proves that laboratory research can make a difference and lead to therapies that help keep people alive," he said.

Dr. William P. Hayes (l) of NICHD explains his poster titled, "Correlated onset of POMC mRNA expression inside and outside the brain: Evidence for embryonic brain-pituitary interactions" to Dr. James L. Olds, NINDS.

Dr. Robert Gallo, chief of NCI's Laboratory of Tumor Cell Biology and one of the speakers at the AIDS symposium, discussed recent advances in the study of Kaposi's sarcoma.

There were two symposia held on Monday and three on Tuesday; all were filled to capacity with standing and sometimes sitting- on-the-floor room only. The symposium on "Gene Transfer and the Potential for Genetic Therapy" held in Wilson Hall was particularly well attended with Dr. Arthur Nienhuis, chief of NHLBI's Clinical Hematology Branch, serving as chairman.

Dr. David Dichek of NHLBI's Molecular Hematology Branch had hand written one of the slides used in his presentation. He joked that when he went to get the artists to do the slide, they had been placed on furlough.

NCI's Dr. R. Michael Blaese spoke on gene therapy for ADA deficiency, and Dr. Steven A. Rosenberg, chief of NCI's Surgery Branch, discussed gene therapy in the treatment of cancer. Dr. W. French Anderson, chief of NHLBI's Molecular Hematology Branch, spoke on the present and future use of gene therapy. Two of these physicians, Blaese and Anderson, 3 days later led the team that performed the world's first gene therapy on a 4-year-old girl with an immune system defect.

Attending several symposia was Dr. Michael Fordis, director of NIH's Office of Education, who said, "The scope of the research demonstrates that at NIH we have a successful marriage between basic science and application in clinical medicine."

The poster session was held in two tents with more than 380 posters displayed during the 2 days of activities. New exhibits were displayed daily with the exception of one poster that drew such a large audience that it was returned by popular demand. Titled, "Scientific Humor and the NIH Scientist," it was presented by Dr. Prince Arora of NIDDK's Laboratory of Neuroscience.

Arora studies how stress affects the immune system, so he thought his humorous poster would relieve some stress. "I just wanted to make them laugh," he said. Arora also presented a poster titled, "Opiate-induced inhibition of calcium flux in immune cells."

"There are just so many things to see and go to," said Bldg. 1's Chen, who paused at Arora's poster. "The festival offers an excess of good things to do."

Agreeing with that were crowds of young scientists trying to attend as many of the symposia and poster sessions as they could.

Dr. Yuan Jiangang, Laboratory of Chemical Biology, NIDDK, was one of those. A visiting associate from China who has been at NIH for 3 years, Jiangang said he had been to the AIDS symposia. While there was not a lot of new territory covered in it, he thought Research Festival was great.

Andrea Cooper, a Fogarty fellow from England who has worked in NIAID's Laboratory of Parasitic Diseases for the past year, said going to the workshops was good. "It is nice to get in touch with other people, have a look around and see what everybody is doing."

Dr. K. Shimoda, a visiting scientist from Japan, has been working for

Dr. John Gallin (l), chairman of this year's Research Festival, presented a photograph of NIH's campus to Dr. Joseph E. Rall in honor of Rall's 70th birthday. Rall serves as NIH's deputy director for intramural research.

NIMH's Laboratory of Biochemical Genetics at St. Elizabeths Hospital for 3 years and has presented a poster for the past 2. He said, "My interest is very limited so I am delighted to talk to anyone who is interested in my field. To find out there are a lot of collaborators out there is a very good thing. Very exciting. This is a big opportunity to discuss my work with top scientists."

Dr. Paul Levine of NCI's Environmental Epidemiology Branch was there with his poster, "The American Adult T-cell Leukemia/Lymphoma Registry (ATLR): Recent Observations." It was his first time exhibiting at the poster session. "It has been very worthwhile. I have been asked very provocative questions that I now have to find out the answers to," he said.

"Very interesting," said Dr. Antonella Farsetti, a Fogarty visiting fellow from Rome, about the poster session. Farsetti has been working in NIDDK's Clinical Endocrinology Branch for 1 year and plans to stay for one more. "I just follow what I'm interested in—thyroid hormone effect. It is always good to know what others are doing so that a door is not closed to you," she continued.

Dr. Reuben Siraganian from NIDR's Laboratory of Immunology, has been at NIH for 17 years and says "Research day, since it started, has been a very good addition to the NIH community."

Executive director and editor of the NIH Alumni Association's newsletter, *NIHAA Update*, Harriet Greenwald manned a booth both days. She reported that people were interested and that NIHAA had picked up some new members. "This is a good opportunity for us to let people at NIH know it (NIHAA) is not just for past employees but also for current employees. We now have more than 1,300 members throughout the U.S. with 450 of those members from the metropolitan area—including Baltimore, Washington, D.C., and Bethesda."

NIH will sponsor the Distinguished Alumni Award annually at Research Festival with the institutes rotating the sponsorship. Next year the National Heart, Lung, and Blood Institute will honor its distinguished alumni.

In 1991, Research Festival is scheduled for Sept. 23 and 24.

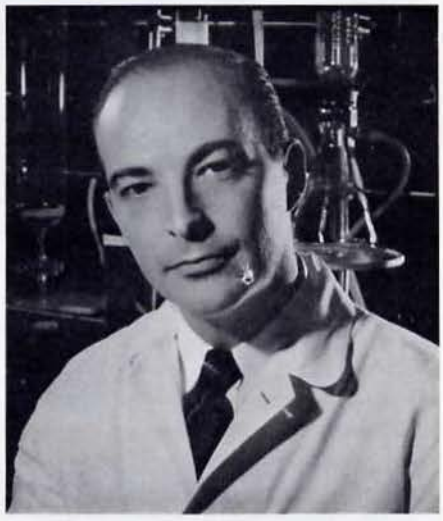
The NIH Distinguished Alumni Award is a replica of the statue "Healing Waters" by Azriel Awret, which is located near the escalator on the first floor of the Bldg. 10 clinic. It will be awarded each year to a distinguished alumni of NIH.

Among the guests at the NCI reception on Sunday, Sept. 9, honoring Drs. Frei and Freireich at the Mary Woodard Lasker Center were (from l) Dr. Alan Rabson, director of NCI's Division of Cancer Biology, Diagnosis and Centers; Dr. Harold L. Stewart; Dr. James A. Pittman Jr., Dean, University of Alabama School of Medicine; and Dr. Ruth Kirschstein, NIGMS director.

Leaving NIH, My Alma Mater

By Dr. Arthur Kornberg

Editor's Note: The following is an excerpt (pages 129-134) from Dr. Arthur Kornberg's book, For the Love of Enzymes. *It crystallizes what many feel about NIH. It is reprinted by permission of Harvard University Press. (Copyright © 1989 by the President and the Fellows of Harvard College.) Kornberg was at NIH from 1942 to 1953 and the excerpt touches upon that period. In 1953 he became professor and chairman of the department of microbiology, Washington University. In 1959 he received a Nobel Prize for the laboratory synthesis of DNA. Currently, he is professor of biochemistry at Stanford University School of Medicine.*



Dr. Arthur Kornberg in 1950

These orotic acid experiments were not the only crossroads I faced in 1953. I had to decide whether to continue at NIH or to veer westward to an academic life at Washington University in St. Louis, a city that would later become my "gateway to the (far) west." The decision to go west was based on two considerations, both of which turned out to be errors in judgment. First, I believed that the advent of the Clinical Center and the disease-oriented institutes would stifle basic research at NIH. And second, I believed that administrative life in a university would be more inspiring than life at NIH. As it turned out, research at NIH flourished, and I learned to my dismay that university administration and politics can indeed be burdensome.

When I came to NIH in the fall of 1942, Thomas Parran, who was then Surgeon General, told me that he wanted his Public Health Service officers less well-rounded but sharper at the edges. So an assignment to NIH promised to be more than the usual two-year military service rotation. While I was still in uniform, NIH sponsored my training in biochemistry with Severo Ochoa in New York in 1946 and then with Carl and Gerty Cori in St. Louis. When I returned in 1947, the Institute had not changed much since the prewar years. But the next year an "s" was added after Institute on the lettering of the Administrative Building architrave, signifying the creation of dental, heart, and other categorical institutes. The Research Grants Division was established, and planning for the Clinical Center was started.

Despite these harbingers of change, the five years between 1947 and 1952 were 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 persuade her that, in working without distraction on problems of my own choosing and digesting biochemistry publications every noon hour with my close friends and colleagues Bernie Horecker, Leon Heppel, and Herb Tabor (whose background and outlook were so like mine), I was enjoying an ideal academic environment.

Few people recognize the NIH acronym, nor do they know of the National Institutes of Health when it is spelled out for them. Yet the achievements of NIH defy exaggeration. It is the prime source of the most extraordinary revolution in biologic science. As expressed by Lewis Thomas: "All by itself, this magnificent institution stands as the most brilliant social invention of the twentieth century, anywhere." More than any university, NIH is my alma mater, and so I feel impelled to interrupt the narrative of this memoir to relate its origins, how it came—to quote Thomas again—"to do something unique, imaginative, useful and altogether right," and to explain why it has been and remains vital for the future of medical science.

In 1987 we celebrated the centenaries of the founding of both the National Institutes of Health and the Pasteur Institute of Paris. Unlike the impressive building, staff, and worldwide recognition the Parisian institute enjoyed at its inception, NIH's beginning was humble in the extreme, a one-scientist, one-room laboratory in the attic of a Public Health Service Marine Hospital on Staten Island. From that start, NIH grew at a modest rate, occupying six small buildings in Bethesda when I arrived there in 1942. Then came the explosive expansion in the post-World War II decades which changed the face of medical science—13,000 people working in fifty buildings on a 300-acre site in Bethesda, along with 52,000 scientists at 1,600 institutions around the world, supported by an annual budget of near $7 billion.

The colossal achievement for which NIH is justly famous is the innovation and maintenance of this vast program of grants for support of research and training in laboratories throughout the world. This program has been the single most important foundation for the biological revolution of the postwar

period. Guided initially by NIH scientists, the peer-review system for awarding grants and fellowships has administered many 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.

Sometimes overlooked is an achievement of NIH that prompted a large group of us to assemble in Bethesda in 1975 for the first alumni reunion. The talk I gave on that occasion tried to express that NIH, more than any college or university, had shaped our lives in the most profound way. In the untrammeled atmosphere of well-equipped, well-managed laboratories, young MDs and PhDs were introduced to professional science. Some remained at NIH, but well over 25,000 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. They are the clinicians in the leading hospitals, 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 factory. NIH is truly a National University of Health.

Looking back at this remarkable success, I am impressed, as an early participant, that this astonishing institution began its development without a plan or the leadership of any one individual. If a proper historical account is ever written, several names and some key policy decisions will be cited. Among the most significant people mentioned will be James A. Shannon, who directed NIH from 1955 to 1968, during which time a 15-fold increase in the budget (from $81 million to $1.2 billion) expanded the broad scientific base of medicine. Representative John E. Fogarty, a bricklayer from Providence, Rhode Island, and J. Lister Hill, Senator from Alabama, were the patron saints in Congress who made this growth possible.

Dr. Arthur Kornberg in 1989

Among the policy decisions, I would emphasize these:

(1) to expend most of the budget extramurally in grants to universities and private research organizations,

(2) to award these grants to individuals, young and old, rather than to departments or institutions,

(3) to make these awards purely on scientific merit as judged by a panel of peers drawn from outside the government,

(4) to be unswayed by political or geographical considerations, national boundaries included,

(5) to support basic research, even within the purview of each of the categorical disease institutes (Heart, Cancer, and so on),

(6) to provide fellowships and grants for training of pre- and post-doctoral students, and

(7) to enlarge the intramural resources (in Bethesda) to accommodate a large expansion of research and postdoctoral training.

Perhaps the most significant of these policies is grant support to individuals selected by peer review. In 1959 I was one of a group of five American biochemists (the others were Konrad E. Bloch, Herbert E. Carter, Bernard D. Davis, and the late Albert L. Lehninger) visiting the Soviet Union as part of an exchange program between our National Academy of Science and theirs. After a month of observing the management of research in the major Soviet universities and institutes, the Minister of Science asked us to compare the Soviet and American systems.

We said diplomatically: "Your system is different. You place authority for direction of research in the hands of a Director. In the United States, the individual scientist is in control. Immediately after completing his training, the young scientist applies for a research grant and is judged in competition with other applicants by a group of peers outside his institution, scientists within his special area of science. With the award of a grant, he becomes his own boss. His success or failure depends on what he accomplishes."

Our Russian host was puzzled: "It is your system that is different," he said. "Our system is the same as that practiced in all other countries, in Europe and Japan." He was right, and it is still true today that in most of the world, direction of research is vested in a relatively few senior people, whereas in the United States the bulk of research money in biology goes to thousands of individual investigators. Some complex problems may require the energies and disciplines of several individuals in a group effort. But far and away, award of research grants to individuals by peer review works best. Progress in science depends on the creative energies of the individual.

An aspect of the NIH grants program which deserves more notice is the award of grants for support of research

*(See **Kornberg** p. 10)*

Kornberg *(continued from p. 9)*
outside the United States. From the very outset after World War II, when funds were inadequate to support all the qualified and deserving American scientists, the decision was made to award grants to the most outstanding scientists and laboratories, regardless of where they were in the world. I am pleased in having had a role in that decision.

The advantages of this international spirit in promoting science proved to be far greater than we expected. In addition, we had not anticipated the enormous boost this altruism gave to medical science and technology in the United States. By rejuvenating European and Japanese scientists and laboratories—in effect a "mini-Marshall" plan for sciences comparable to the massive postwar Marshall plan for economic rehabilitation—we were able to enlist the vast reservoirs of talent on all three continents. In so doing, knowledge was obtained which we could all share and thereby generate the most remarkable advance in medical science the world has ever known.

As a consequence of the rebirth of science centers in Europe and Japan, a tide of gifted students and senior investigators flowed into the United States. We welcomed them, and many remained to enrich American universities, research institutes, and industries. At the NIH laboratories in Bethesda alone, many thousands of foreign scientists (over 3,000 from Japan alone) received postdoctoral training and became loyal alumni upon returning to their native countries. These developments also helped to create markets for American technology and pharmaceutical products and to establish English as the international language of science.

Were the NIH record to be described for publication as an experiment in research administration, an impartial reviewer, even in this social area of science, might well question whether other factors might have been responsible for the good result. Such an experimental control does in fact exist in the support program of agricultural science in the United States during the same postwar period. The Department of Agriculture retained all authority within its own bureaucracy and limited research activity to its few established regional laboratories around the country. There were no grants to universities and private institutes. With this old-fashioned system of management, the knowledge base for agriculture remained stagnant. Little was learned about the basic biochemistry and genetics of plants and farm animals. Only recently, with the introduction of recombinant DNA technology, has there finally been a slight awakening of interest and activity in basic agricultural science.

Dr. Arthur Kornberg and Dr. DeWitt Stetten Jr. in 1959

The Alumni reunion of 1975 was held not for sentimental reasons, nor to publicize past and present achievements, but rather to express the concern of alumni for the future of NIH. Despite its superb record and its dedication to science and the conquest of human disease, NIH had become and remains the target of budget cutters and antiscience forces. As with all worthwhile things, the struggle for survival is never won. This is even more true of support for science than of support for other institutions in society.

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 failure can be seen among members of the lay public, political leaders, physicians, and even scientists themselves. Most people are not prepared for the long time-scale of basic research and the need for a critical mass of collective effort. Fragments of knowledge unwelcomed and unexploited are lost, as were Gregor Mendel's basic genetic discoveries. The vast majority of legislators cannot accept the seeming irrelevance of basic research. Were there a record of research grants in the Stone Age, it would likely show that major grants were awarded for proposals to build better stone axes and that critics of the time ridiculed a tiny grant to someone fooling around with bronze and iron. People do not realize that when it comes to arguing their case for more funding, scientists who do basic

research are the least articulate, least organized, and least temperamentally equipped to justify what they are doing. In a society where selling is so important, where the medium is the message, these handicaps can spell extinction.

NIH Grantees Win Nobel Prizes

Dr. Elias Corey Wins in Chemistry

Dr. Elias J. Corey of Harvard University, who has been a grantee of the National Institute of General Medical Sciences for 20 years, is the winner of the 1990 Nobel Prize in Chemistry. Corey was cited for "his development of the theory and methodology of organic synthesis." For many years, his laboratory has been outstandingly successful in the synthesis of a varied array of drugs and other complex molecules of biological interest.

One of Corey's most recent achievements is the development of a family of totally synthetic enzymes that he calls "chemzymes." *Science* magazine has called these molecules "among the most intriguing innovations of the decade."

Chemzymes are small molecules that catalyze certain reactions quickly and in such a way that only the biologically effective product is made. Moreover, they are produced by "rational" molecular design—that is, Corey and his coworkers start out by understanding the chemical mechanisms involved in a particular reaction and then synthesize molecules with exactly the properties needed.

Conventional chemical synthesis of biologically active molecules results in a product containing molecules that are mirror images of each other—so called "right-handed" and "left-handed" molecules. A molecule of the wrong "handedness" is usually either useless or may even cause serious side effects. Chemzymes, in contrast, make every one of their product molecules in the same orientation. This eliminates not only the waste of costly raw products at the beginning of a synthesis, but also eliminates the need to remove unwanted products of the wrong orientation at the end of the synthesis. The use of chemzymes will thus help synthetic chemists eliminate one of the most persistent roadblocks to efficient, cost-effective chemical synthesis.

NIGMS has also supported Corey for many years to develop sophisticated computer techniques with which chemists can work interactively to synthesize organic compounds. In addition, he recently received an NIGMS MERIT award, which provides for extended support to foster the continued research achievements of distinguished scientists.

Since 1962, NIGMS and four other NIH institutes—NCRR, NCI, NHLBI and NIAID—have awarded Corey 58 grants and contracts totaling $12,059,338.

Drs. E. Donnall Thomas and Joseph E. Murray Win In Medicine or Physiology

Drs. E. Donnall Thomas and Joseph E. Murray, who shared the 1990 Nobel Prize in Medicine or Physiology for pioneering transplant therapy in humans, are both longtime NIH grantees. Thomas was on campus for Research Festival 1990 in September; he lectured on marrow transplant as a therapy for leukemia.

An investigator at the Fred Hutchinson Cancer Center in Seattle, Thomas, 70, has been an NIH grantee continuously since 1953. Institutes supporting his work have included NCI, NIAID and NIDDK. He has received grants from PHS totaling more than $65 million in his career, said Robert F. Moore, head of DRG's special projects and presentation unit.

"Thomas was also a member of a cancer study section in the late sixties and early seventies," Moore continued.

Murray, 71, a professor emeritus at Harvard Medical School, received funding of more than $3 million during the period 1956-1973 from NHLBI and NIAID.

The work for which the scientists were honored began in the 1950's, at about the time they began winning NIH grants.

"We did recognize the two of them early on," Moore observed.

The researchers will share a prize of $703,000.

Children's Inn Needs Weekend Volunteers

The response to the Children's Inn has been magnificent. However, there is one need for which the inn still lacks the necessary response—weekend coverage.

This contribution means arriving at the inn by 6 p.m. Friday and taking the place of the resident manager until 6 p.m. Sunday. Volunteers get a training orientation from Kate Higgins, resident manager, as well as written house instructions. In case of emergency, help from a staff person is just a beeper away.

There are several attractions to this service. Not only are you helping others in need, but you are also spending a quiet weekend in a beautiful country inn. Most patients' families are back at their own homes for the weekend and the atmosphere is quiet and relaxed. There just needs to be someone "in charge."

Since weekend volunteering means not leaving the property, it is much more fun to share this weekend with your spouse or a friend. That way, one of you can leave while someone is still in residence. If you are interested in helping out, call Pam Keller, (301) 496-5672.

'A Dream Come True'

Children's Inn Opens Amid Fanfare, Celebrations

By Rich McManus

Nine years of hoping, 2 years of building, and 4 years of high-level corporate and political lobbying culminated in the opening of the Children's Inn at NIH during the third week of June.

"Can you believe in Washington, D.C., that talk became a reality?" marveled congressional wife Debbie Dingell, who was master of ceremonies at the inn's June 21 ribbon cutting. Her husband John represents Michigan in Congress. One of several congressional wives whose energy and effort helped the 9-year dream come true, Mrs. Dingell presently serves as vice president of the Friends of the Children's Inn. "For once we've done something grand," she continued. "Ultimately, the inn will become a place of encouragement, empowerment and hope."

Festivities began Sunday, June 17 with an open house and reception for workers who built the inn, local community members and children. Mickey and Minnie Mouse were surprise guests at that affair. The celebrations ended the following Friday night at a dinner for bereaved families and friends of the inn's operations board.

In between, President and Mrs. Bush stopped by for 45 minutes on Thursday morning, more than 3,000 employees toured the 33,000-square-foot residence on Tuesday afternoon, and two separate ribbon-cuttings took place. This in addition to a lavish catered dinner for corporate donors Wednesday night put on by Merck & Co. Inc., which donated some $3.7 million—the company's largest charitable gift ever—toward construction of the building.

"I've been so impressed by what I've learned about the unique concept of the Children's Inn," said Bush. "It's an extraordinarily sensitive idea. I am very moved to be here to see how joyously your caring has been realized."

Helping children cut the ribbon to open the Children's Inn at NIH on June 21 were (from l) Barbara Bush, Merck chief Dr. P. Roy Vagelos, President Bush, and HHS secretary Dr. Louis W. Sullivan.

Intended to be a national model of family and child-centered care, the inn will provide room for up to 36 families that have children being treated on pediatric protocols at NIH. Some 60 percent of the residents will be cancer patients; the remainder will be here for a host of childhood illnesses including heart disease, osteogenesis imperfecta (OI, or brittle bone disease), epilepsy, asthma and arthritis.

Bush picked OI patient Brianne Schwantes of South Milwaukee as an example of the value of family-oriented care.

"Those who have treated her say that it is her family's depth of support that has given this child her life," he said. "The family is the key to everything."

Endorsing the first lady's recent admonition to the graduates of Wellesley College to put family first, even if it means sacrificing career goals, Bush said, "The lesson of the inn will show us all that the most important part of life is a very simple one—sharing a laugh, wiping a tear, listening to a loved one."

Bush singled out Dr. Philip Pizzo, chief of NCI's Pediatric Branch and so-called "godfather" of the inn, and Dr. P. Roy Vagelos, chairman and chief executive officer of Merck (and an NIH intramural scientist for more than a decade) as "people of exceptional goodness." He also thanked parents and nurses: "You have a special grace. You bring joy and strength to each other."

Reciting the Prayer of St. Francis of Assisi, Bush concluded, "God bless this place," then set about cutting the inn

ribbon with a crowd of children. Both the president and first lady then spent a good while greeting and hugging children and posing for pictures with parents.

Ceremonies earlier in the week were characterized by passion and joy.

"Acting NIH directors aren't allowed to have many happy occasions," joked Dr. William Raub at the Tuesday ceremony, "but believe me, I'm going to enjoy this week."

Emphasizing that the inn will enrich the research mission of NIH, Raub said, "The Children's Inn can't quite be a home in the literal sense, but it can come close."

"One day the inn will be a monument to the children whose participation in research projects allowed diseases to be cured," predicted Pizzo. "These cures we hope for will allow children to stay in the real inn—their homes."

HHS secretary Dr. Louis Sullivan, who was here Thursday with the president, called the inn "a wonder of the human spirit, a wonder of generosity and giving, and a wonder of caring and curing. It is the product of an inspired, intrepid and indomitable group of people."

Merck chief Vagelos said the inn was but one example of the "extraordinary advances that can result when private industry cooperates with public institutions."

Addressing the gathering Wednesday evening, Vagelos particularly credited Carmala Walgren, wife of Rep. Doug Walgren of Pennsylvania, with spearheading the inn's creation.

"Carmala was catalytic in getting this thing going," he said. "She is a very determined lady, a compassionate mother and a very good lawyer. She was very persuasive. Dogged, I would say."

Vagelos praised two other congressional wives for their "countless hours and enormous effort"—Dingell and Chris Downey, wife of Rep. Thomas Downey of New York.

"Nature is not always just," observed Downey, "and we are here because we want justice done."

Walgren, who became involved in the Children's Inn early in 1986 when a neighbor fell ill with cancer and was treated here, called the inn "a work of love, an example of the importance Americans place on family."

When the first families to occupy the inn arrived on July 2, they were greeted by a structure that some 3,000 NIH employees had seen and admired during an open house that was tagged onto the traditional Camp Fantastic fundraising barbecue on June 19 (and which raised a record $5,500 for the camp for children with cancer).

"We wanted this house to be an extension of the healing process for kids and families," said inn architect Bob Greenberg. "The objective is to encourage families to interact and to get out of their rooms."

Greenberg and building director Alan Kay of Alan I. Kay Companies wanted a structure that was unlike the imposing medical setting of the Clinical Center. They selected such noninstitutional materials as wood-shake shingles, cedar siding, stone, copper and glass, wood planter boxes, copper gutters and downspouts, and stone arches to get a residential feel in keeping with an upscale Bethesda neighborhood.

While the outside of the inn suits the 2-acre wooded site donated by NIH (and chosen from among several rustic campus parcels), the inside of the inn is the heart of the facility.

A magnificent community room dominates the entryway of the inn, anchored by a stone fireplace whose chimney, 8 feet in diameter, rises 2½ stories through a skylight in the roof. Pastel and earth-tone furnishings and carpet are set off by white oak railings and trim. Banks of greenery built into the floor accent the margins of the room. A sculpture donated by Merck

*(See **Inn** p. 14)*

A stone chimney 8 feet in diameter dominates the inn's community room, here being inspected by employees during an open house June 19 for NIH'ers. The fireplace includes a natural gas ignition system.

Inn *(continued from p. 13)*
graces the entryway.

Other common areas include a glassed-in playroom offering easy monitoring by parents and an adjacent play terrace. Each area includes seating for parents, a feature that inn executive director Andrew R. Tartler calls essential for maximum use.

"Studies show that play areas are used more frequently when parents have a place to sit," he said, indicating the care that went into even small details of the inn.

Sliding glass doors and screens in the play terrace admit some of the outdoors to the inn, a factor Tartler calls important when many pediatric patients are not permitted to play outside.

Toys and gadgets, including 35 miniature wooden airplanes donated by students at Baker Intermediate School in Damascus, are designed for "successful play," Tartler continued, defining this as play that accommodates all levels of ability.

Cork-backed flooring in play areas minimizes chances of injury due to falls, he added; a playground designed by the same architect who planned the Cabin John Regional Park play area will be built behind the inn in the future.

The second floor of the inn includes the residential section—four "pods" (A,B, C and D) containing nine suites, six of which are interconnecting (in case of visits by extended family). Each room sleeps four adults comfortably. All rooms include a bath and private phone (though phones for free long distance calls are located in each pod) and one room in each pod is completely wheelchair-accessible.

Two rooms come with kitchens in the event of long-term stays and two rooms have sliding glass doors leading outside. Ceilings in each room are a capacious 9 feet high.

"Some families might not want to stay here," allows Tartler. "There can be a magnifying effect when so many people in the same situation are put together." Other potential residents might object to house rules such as no smoking or alcohol consumption. For these people, NIH will continue to provide subsidized lodging at area hotels and motels.

A number of congressional wives devoted great energy to get the inn built. Among them were top officers of the Friends of the Children's Inn, Inc. (from l) D. Chris Downey, secretary; Debbie Dingell, vice president; and Carmala Walgren, president.

Other inn amenities include two community kitchens with shelf and cabinet space for each family. Families, who stay for free but are asked to make a minimum donation of $10 per night, must buy their own groceries; the inn provides only minimum refreshment. For purposes of hygiene, the dishwashers in each kitchen are equipped with a sanitation cycle. Also, icemakers are fully automatic, meaning that no dirty hands go fishing for loose cubes.

Meals can be eaten in two dining areas, each skylit and open to the kitchen via pass-throughs. The dining rooms also open onto covered outdoor terraces furnished with tables and chairs.

Overlooking the chimney-dominated community room is a large television room with a big-screen color TV connected to the local cable (all rooms have cable access as well). Immediately adjacent is a solarium that also has a TV; parents are expected to use this room when a mellow PBS broadcast suits their mood more than blaring MTV.

Past the TV rooms is a glassed-in computer room. Five personal computers will allow children to keep up with homework, play video games or keep in touch with a relative back home who also has a computer.

Returning to the first floor, there are two quiet rooms for small meetings, a teen room for pinball games and socializing, a library/conference room, an information/administrative office and a lounge for volunteers.

Since the inn has only 4 paid staff, dozens of volunteers are needed to conduct orientations and operate the inn on a day-to-day basis. Presiding over the house is resident manager Kate Higgins, who has an apartment just to the right of the inn's front door.

Admission to the inn will be coordinated first by a social worker and subsequently by parents or guardians of children participating in NIH protocols. Preference will be accorded to children who are most ill. Age range will be 0-18, with some leeway for young adults.

"We might take someone as old as 25," said Tartler.

The NIH campus shuttle system now includes stops at the inn. The inn also has a shuttle bus of its own to accommodate the shopping needs of residents.

While NIH will contribute laundry service, electricity, and shuttle service, in addition to the land it has already given, funds for operating costs are still being collected. An endowment of some $7 million is being sought, said Randy Schools, general manager of R&W and the only person to sit on both the inn board, which operates the inn, and the board of the Friends of the Children's Inn, which is the fundraising arm.

"So far we have raised $5.4 million," Schools said.

"We hope eventually to raise about $7 million, but that's a long way off. It would be nice if one day we could use the interest on that money to cover operating expenses for the inn."

"More than 4,000 people have already contributed their energy, money, love and support to this project," said Kathy Russell, president of the inn board.

Said Cindy White, whose daughter is an NIH patient and who also sits on the inn board, "This home will have a beautiful impact on countless children."

No one who has seen it can doubt her.

Children's Inn Had a Predecessor on Campus

While the Children's Inn at NIH is, in many respects, unique, it is not the first residence for ill children on the NIH campus.

Back in 1957, on the present site of Bldg. 37 west of the Clinical Center on South Drive, a 2-story house called the Children's Treatment Residence opened. Occupied by six boys ages 10-12, a housemother and a live-in counselor, the residence was built for use in NIMH's research on emotionally disturbed children.

"The house was built for children with severe behavior disorders," remembers Hazel Rea, deputy director of NIMH's intramural research program. "The patients were among the earliest occupants of the Clinical Center, but they were just awful to have in a hospital. They would disconnect all the wires on the machines so that you didn't know what wire went where."

The Treatment Residence offered the opportunity to examine the effects of an "open setting" of living arrangements as opposed to the closed setting of a hospital ward.

"It was the brainchild of Dr. Fritz Redl," said Rea. "His idea was that these children needed 24-hour treatment in a residential situation. These were impulsive, acting-out children. The theory was that you dealt with their behavior on the spot. Tackle it right then and there, rather than talk about it later.

"I think it didn't last very many years," said Rea. "It's really not very comparable to the Children's Inn."

This photograph is from the Prints and Photographs collection at the National Library of Medicine. The curator, Lucinda Keister, would like more information about it, especially the year. The photo was taken when NIH employees were interviewed by WTOP radio in the cafeteria in Bldg. 1. The program was part of a series transcribed at government cafeterias in the Washington area. Does anyone remember the year this took place and the name of the interviewer? We have identified Dr. Evelyn Anderson, Dr. Irvin Fuhr, Hope Norris, Alex Adler, Virginia Burlingame, Dr. Morris Belkin, Dr. Stella Deignan, Roy Perry, Ariel Clark, and Catherine Schellack. Please send information to *Update*.

Parity Among Sexes Sought

New Women's Health Office at NIH Announced

By Carla Garnett

NIH has created a new office devoted entirely to research on women's health issues. Named the Office of Research on Women's Health, the new entity will help establish parity among the sexes in biomedical research.

"The Department of Health and Human Services and the NIH recognize the need to include women in clinical studies and to be attentive to women's health concerns," said NIH acting director Dr. William Raub, who announced the creation of the new office at a recent roundtable meeting of DHHS and NIH officials and members of the Congressional Caucus for Women's Issues.

"The NIH will take all the steps necessary to ensure that appropriate numbers of women are included in research projects," he said.

The new office comes to NIH amid criticism from some members of Congress that the institutes have not studied adequate numbers of women in clinical trials.

Criticism stemmed in part from a July 1990 General Accounting Office report that NIH had been slow to implement a policy published originally in the 1986 *NIH Guide to Grants and Contracts*. The policy suggested by the NIH advisory committee on women's health issues, informed grant applicants of the need to include women in clinical trials.

Raub announced plans for several measures that will immediately address the concerns of Congress and GAO.

One measure has already been implemented: *The NIH Guide to Grants and Contracts* now includes a revised announcement to would-be grantees that numbers of women in clinical trials should be proportionate to numbers of women with the condition under study.

Raub said NIH's new efforts toward women's health will include enhanced research activities by all institutes and will be intramural as well as extramural.

Raub's announcement warns grantees: Have "compelling justification" for excluding women from the study, or forfeit the NIH grant.

"Failure to provide gender information about proposed studies will result in deferral of the application," he said.

Dr. Ruth L. Kirschstein

In addition, required training sessions have been scheduled on seven different occasions to inform NIH personnel who handle grants of these new policies.

Rep. Patricia Schroeder (D-Colo.), cochair of the Congressional Caucus for Women's Issues, applauded the new NIH actions.

"I think we're going to find in the future that it will be much easier to keep track of and see what kind of progress we're making," she said. "I think it shows the dedication of NIH and how well they were listening."

Schroeder recently advocated an increase in national obstetric and gynecological research.

"Women are more complex (than men) and therefore the studies, according to GAO, become all the more important," she said. You can have women who are pregnant and nonpregnant. You can have women pre-, post- or menopausal. All those states could require different types of treatment."

According to Sen. Barbara Mikulski, who introduced the Women's Health Equity Act in Congress Aug. 2, women have been shortchanged long enough.

"When one looks at medical practice, the facts are frightening," she said. "Women's health needs have either been ignored or our life processes—like birth and menopause— are often treated like diseases rather than natural processes to be studied, helped and assisted. Often our life processes are minimized or trivialized."

Schroeder said primary caregivers for women need the results of gender-specific research to direct them.

"(Without it), they are really flying blind," she said. "And that's been happening a lot as we look at the research."

One often-cited example of medical research results that differ among men and women is the 1981 NHLBI study of 22,000 male physicians.

That study found that men reduced their incidence of heart attacks by taking an aspirin every other day. Because the study involved no women, the preventive aspirin strategy may or may not be applicable to females.

"It's all a very well-kept secret that the number one killer of women in America happens to be heart disease," Schroeder said. "Sometimes I think there's been a myth out there that we're all healthy. But when you look at the statistics, we're not.

Raub said the majority of NIH's research is not gender-specific, but equally relevant to both sexes.

"The bulk of our clinical research is and should be applicable to both genders as is the fundamental basic science that makes those clinical research opportunities possible," he said.

NIGMS director Dr. Ruth Kirschstein echoed Raub's sentiments, citing an NCI colon cancer study that included women in numbers appropriate to the disease's prevalence in females.

"Unfortunately, colon cancer kills more women annually than all gynecological cancers combined," she said.

Kirschstein, who has been named acting associate director for research on women's health and will lead the new office on women's health until a permanent director is found, is cochair of the PHS coordinating committee on women's health issues.

"One goal of the Office of Research on Women's Health is to determine what research, intramurally and extramurally, may relate specifically to diagnosis, treatment and prevention of diseases in women," she said.

"The office will maintain an ongoing dialogue with the scientific community and with women's health advocates and will communicate their concerns to the director of NIH and to the directors of the various institutes, centers and divisions."

The new office will develop a trans-NIH plan to keep track of NIH-funded research of all diseases and conditions that affect women, she said.

Rep. Connie Morella (R-Md.), who represents Montgomery County in the House of Representatives and this year sponsored the Women and AIDS Outreach and Prevention Act, called for a special effort to increase the numbers of women in AIDS studies.

Representation of women in clinical AIDS studies critically trails representation of men, she said.

"We know that the federal response to the AIDS epidemic has been appropriate in terms of men—appropriate for the decade of the nineties—but the response to the epidemic in women lags about 10 years behind," she said.

"Statistically it's rather frightening that women now comprise the fastest growing group of people with AIDS," Morella continued.

In New York City, AIDS has become the leading cause of death for women ages 20 to 40, she said.

"So often women have been looked at as transmitters of the disease to men and to children without being looked at as entities unto themselves," she said.

Mikulski summed up the concerns of the caucus: "We want to be sure that research is translated into action, prevention, outreach, public education—not only of consumers but also of physicians who deliver service.

"This isn't a one shot deal," she continued. "This is a commitment to be sure that, when we go into the 21st century, we go in practicing 21st century medicine, but not with 14th century attitudes."

If your present address differs from that shown on the address label, please send your new address to 9101 Old Georgetown Rd., Bethesda, MD 20814.

CALENDAR

DECEMBER

An exhibit on "Public Health in New York City in the Late 19th Century," commemorating the centennial of the publication of Jacob Riis' *How the Other Half Lives* is now on display in the lobby of NLM, where it will continue until Dec. 28. The library is open 8:30 a.m. - 9 p.m. Monday - Thursday and 8:30 - 5 p.m. Friday - Saturday. For more information call (301) 496-5405. Single copies of a booklet bearing the same title as the exhibit may be obtained without charge by writing: Chief, History of Medicine, National Library of Medicine, 8600 Rockville Pike, Bethesda, MD 20894 (please include a self-addressed label).

JANUARY

The G. Burroughs Mider Lecture will be Jan. 16, 1991, at 3 p.m. in Masur Auditorium, Bldg. 10. The speaker will be Dr. Mortimer Mishkin, chief, Laboratory of Neuropsychology, NIMH. His topic will be "Memory Circuits."

For information about various lectures and events at NIH, you may call (301) 496-1766 and for NIHAA (301) 530-0567.

IN OUR NEXT ISSUE. . . .

Articles on 1990–the year in review at NIH; the new AIDS facility at the Clinical Center; NIH discoveries, 1930-1945 and the NIH budget. Also there will be our continuing features: NIHAA Forum, NIH Notes, Science Research Updates and news from and about NIHAA members.

Pays Tribute to Pratt

New Computer Exhibit Added to Stetten Museum

By Anne Barber

A new exhibit, "Computers in Medical Research," was recently added to the DeWitt Stetten Jr. Museum of Medical Research. The exhibit is located near the patient elevators on the first floor of the Bldg. 10 clinic. Opening ceremonies on Oct. 17 combined a symposium on computers in medical research with a tribute to Dr. Arnold W. "Scotty" Pratt, the first and only director of the Division of Computer Research and Technology since its origin in 1966 until Pratt's recent retirement this past June. Pratt was paid homage by many of his colleagues and friends at NIH.

"DCRT, in its every essence, is the house that Pratt build," said Dr. William F. Raub, NIH acting director. "It is tangible and durable. It was because of Scotty's foresight and commitment that DCRT moved ahead.

"Computers need to serve medicine, and medicine should serve people—that is what NIH and Scotty Pratt are all about," Raub stated.

Pratt came to DCRT from the National Cancer Institute, which he joined in 1948 as head of the energy metabolism section in the Laboratory of Physiology. In 1948, computing did not exist, even as a punchcard operation. Pratt's research at NCI led him to investigate a number of biomedical research areas to which computers might be applied. He subsequently published several papers on computational analysis of ultraviolet absorption spectra and the use of computers in cancer chemotherapy.

At Pratt's retirement, 42 years later, biomedical research at NIH had made major strides and computers have become an integral part of biomedical

NIH historian and curator of the DeWitt Stetten Jr. Museum of Medical Research Dr. Victoria A. Harden (l) presents Dr. Arnold W. Pratt, director of the Division of Computer Research and Technology from August 1966 to June 1990, with a miniature copy of the poster displayed in the exhibit.

programs and administrative procedures, with more than 5,000 personal workstations campus-wide and an $800 million central computer facility.

Today, DCRT not only has primary responsibility for incorporating the power of modern computers into biomedical programs and administrative procedures for NIH, it also serves as a scientific and technological resource for other parts of the Public Health Service, and for other federal components with biomedical and statistical computing needs.

Dr. William C. Mohler, deputy director of DCRT, remembers Scotty as a pioneer in the true sense of the word—he explored the use of new instruments along with computers. "He was also a developer," said Mohler. "He was told by Shannon (former NIH director Dr. James A.) to 'Go build a DCRT.' And that he did." In his response, Pratt said, "The exhibit tells the story. There is much for all of us to be proud of. I'm so glad that I had a great staff there with me in the minimum security detention center that we call DCRT. Shannon believed the job of NIH was to conduct and sponsor research. And since there was no computer vendor that could provide what Shannon wanted, he said, 'You go and do this, and earn your way on a fee-for-service basis.'" Turning to Dr. David Rodbard, the newly appointed DCRT director,

Pratt gave this message: "I leave you with some images to live up to, but I also leave you with one hell of a staff and you will need them." Dr. Thomas Lewis, chief of the Clinical Center's information systems department, spoke on "Medical Informatics, Medical Care, and Medical Education." He stated that Scotty had been his mentor since 1971 when he joined NIH.

"When Scotty began, there were no experts in the computer field. Now they are becoming increasingly specialized, which is essential to NIH's environment. Scotty's theory—'Get rid of those punchcards and make information systems easy to use'—was good news to the CC, which is data intensive," continued Lewis. "With 17 floors and 6 miles of corridors, we really need information systems."

Dr. Daniel R. Masys, director of the Lister Hill National Center for Biomedical Communications, spoke on "Computing in the Future: Visualizing the Virtual Library." Stating that no cards have been added to NLM's catalogue division since 1980, Masys said, "And none will ever be added again. Everything is now done on microcomputers.

"This was all unforeseen 30 years ago. During the past 30 years we have seen computers woven intimately with patient care. Today, however, the game is changing. New science and new technology equal new opportunities." He said computational biology, which compares patterns of molecules, and the human genome project, with its long DNA sequences, make this the era of images.

NLM is building a digital image library that would have a complete set of x-y-z numerical coordinates representing the internal and external structure of an entire human being at millimeter-level resolution. This "Visible Human" project would yield a computer data set of unprecedented detail and form the basis for a virtually unlimited number of image renderings of the human body. But, he states, "We have far to go to make it usable by our professional colleagues."

Dr. Arnold W. "Scotty" Pratt

Masys closed with an old Chinese proverb: "Tell me and I will forget, show me and I may remember, involve me and I will understand."

Rodbard, following in Pratt's footsteps as the new DCRT director, said he considers himself very fortunate to have been working with Scotty in 1966 when computer use at NIH took off. "However," he stated, "as exciting as it's been over the last 25 years, it will be equally or more exciting in the next 25."

Rodbard compared DCRT's future to riding two ocean waves at the same time, each accelerating with growth. One wave is the computer with its hardware and software, and the other is biomedical research. "We need to harness these two waves and make them into one," he says.

In closing, Rodbard said, "I am looking forward to going onward from here. My hat's off to Scotty and the entire DCRT staff."

Dr. Victoria A. Harden, NIH historian and curator of the Stetten Museum, presented Pratt with a miniature copy of the poster used in the exhibit as a memento of the occasion.

After a standing ovation from the crowd, Pratt and his many friends and colleagues attended a reception held immediately following in Bldg. 10's Visitor Information Center.

The exhibit was produced by the Stetten Museum in collaboration with the NIH Division of Computer Research and Technology, the National Library of Medicine, and the Warren Grant Magnuson Clinical Center.

This exhibit, "Computers in Medical Research," is part of the DeWitt Stetten Jr. Museum of Medical Research, which collects and exhibits biomedical research instruments and other artifacts relating to NIH history.

Endocrinologist, Mathematician, Statistician

Meet the Newest Institute Director, Dr. David Rodbard

By Anne Barber

Dr. David Rodbard became the director of the Division of Computer Research and Technology on Nov. 5. He succeeds Dr. Arnold W. Pratt, DCRT's first and only director until retiring last June.

"I would like to see an increase in scientific computer applications that would assist scientists in labs/clinics as well as statisticians and epidemiologists throughout the NIH community," he said. "This will involve personal computers, workstations, mainframes and supercomputers."

One of the major functions of the computer center, Rodbard points out, is to serve as the focal point and coordinator of all computer activities on campus. "And, we have many diverse systems," he adds.

"We want to encourage more interactions with all groups at NIH including the Clinical Center, National Library of Medicine, Lister Hill Center, National Center for Research Resources, and NCI's Advanced Scientific Computing Laboratory in Frederick, as well as all computer facilities on campus, large or small." In addition, Rodbard wishes to maintain and further develop advanced research in biomedical computing with emphasis on molecular graphics and dynamics, the biophysics of molecular interactions, the analysis of nucleic acid and protein sequence data leading to the prediction of secondary and tertiary structure, and imaging on both the clinical and molecular levels. "I have a great deal of respect for the high level of expertise in DCRT and plan to continue the many effective programs and services," he said. The Computer Center Branch has provided consistent, reliable, economical service on the central mainframe facilities, among many other activities. The Data Management Branch has developed and supported the administrative data bases essential to the operation of NIH, both intramural and extramural.

"I feel that the tremendous talent within DCRT can better serve the NIH community by establishing close links with multiple labs throughout NIH. We can assist with the computer automation of labs throughout the campus."

The task of computerizing biomedical research is so large that DCRT cannot do it alone, he admits. "Acting as a reservoir of expertise and a resource for training, DCRT can provide support for user groups and serve as the hub of the network that will link all scientists at NIH with each other and the outside world." In the near future, Rodbard sees the networks RESnet and NUnet having a tremendous impact on NIH scientists.

Dr. David Rodbard

The recent establishment of the Enter Bulletin Board System allows scientists to talk to one another almost instantly and effortlessly, he points out. "This means they can share reagents, cells, antibodies, isotopes, even transgenic animals, that may lead to considerable cost savings in this era of austere budgets."

Rodbard would eventually like to see a listing by author, title and keywords of all abstracts, manuscripts, and publications by NIH scientists entered into BBS at the same time they are submitted for clearance for publication. This would enable other NIH scientists to have access to the information 6 to 12 months in advance of publication.

"Working together with NLM and Lister Hill Center, we could perhaps adapt Grateful Med software to retrieve this type of pre-publication information," he continued. "I am sure NIH scientists can conceive other important uses for BBS and the networks."

DCRT's Computer Systems Laboratory has been a leader in the development of advanced laboratory work stations and associated software including a lab analysis package. "This is just the beginning of the development of tools for use by bench scientists at NIH," he said.

Rodbard sees the large biometrics/epidemiological community at NIH as an important ally for DCRT, both in terms of its expertise in statistical computing and in providing consultation in experimental design/data analysis. This group of scientists has developed considerable computer expertise of its own and DCRT would like to join it in a number of ventures.

"Certainly biomedical research is moving faster than ever before," he observed. "Likewise, the development in computer hardware systems and software is moving at a fantastic pace." The job of DCRT, he says, is to harness these two developments in order to provide practical assistance to all scientists.

When Rodbard joined NCI back in

1966 as a clinical associate in the Endocrinology Branch, he worked closely with DCRT especially in mathematical modelling of radioimmunoassay and receptor binding data.

"I had the good fortune to learn my way around DCRT rather quickly," he said. "I came here for assistance as well as to use the superb central facilities. I would like to make it possible for more scientists to exploit the resources of DCRT to help facilitate their research as much as DCRT facilitated mine. I'm convinced computer networking will have a tremendous benefit for all aspects of life at NIH," he said.

Another of Rodbard's goals is to explore possible collaboration with a wide range of outside institutions including universities, other federal government agencies and industry. He would also like to expand DCRT's involvement internationally by bringing recognized scholars to DCRT through the auspices of the Fogarty International Center.

"The computing scene changes so rapidly," he says. "It is very important for us to stay in touch with the world to stay abreast."

Rodbard is also interested in expanding the summer program for students to encourage careers in biomedical computing and to reach minorities and persons with special needs.

DCRT's Personal Computing Branch, according to Rodbard, has had a tremendous impact on providing support and consultation to users of PCs at NIH. "We would like to see this kind of support enhanced, especially in high level scientific application areas, with more sophisticated software."

Prior to becoming DCRT director, Rodbard served as chief of NICHD's Laboratory of Theoretical and Physical Biology and head of its theoretical biology section. He also served as coordinator of the Clinical Center's "Computers in Clinical Medicine" elective course from 1981 to 1989.

"In this capacity," he said, "I developed a faculty of more than 70 scientists drawn from all the institutes plus DCRT and the Lister Hill Center. This provided me with a fairly high degree of familiarity with computer activities in the area and brought me into close contact with all laboratories and branches of DCRT."

His interest in mathematical statistics and biophysics using computers to solve problems, especially in the area of endocrinology, led Rodbard to develop a number of computer programs that have been distributed and used throughout the world. Examples include the Logit-Log method for radioimmunoassay; the FLEXIFIT and the ALLFIT methods for analysis of families of dose response curves; and LIGAND for analysis of receptor binding data. The latter two programs were developed in collaboration with Dr. Peter Munson of NICHD and Dr. Andre DeLean, a former NCI fellow. One of the papers written by Munson and Rodbard has been cited nearly 2,000 times and has been listed as one of the 300 most-cited articles in the world in biomedical literature.

Rodbard, a member of the PHS commissioned corps, earned his M.D. in 1964 from Western Reserve University School of Medicine in Cleveland. He received his B.A. degree, magna cum laude, from the University of Buffalo in mathematics and chemistry.

An author or coauthor of more than 260 publications, Rodbard also serves as board member and treasurer of the Foundation for Advanced Education in the Sciences. He is an active member of the American Society for Clinical Investigation, American Physiological Society, American Society for Biochemistry and Molecular Biology, American Statistical Association, Biometrics Society, the Endocrine Society, and the American Diabetes Association and others.

"I am very proud and honored to have been appointed to this position," says Rodbard. "And I look forward to the many exciting developments of the next decade as we prepare for computing in the 21st century."

In accordance with construction tradition and lore to assure good luck, an American flag and a lone cedar tree sit atop the Child Health and Neurosciences Bldg. 49 before the roof is finally topped. Bldg. 49 is the first new building on campus in 10 years and it is scheduled for completion in late 1992.

NIH Claims Ten Percent of Decade's Hundred Most-Cited Scientists

By Carla Garnett

Intramural NIH has distinguished itself in one of the most competitive areas of biomedical science—publication of research. According to a recent issue of *The Scientist*, ten NIH researchers are among the top hundred most-cited scientists of the 1980's. The list was compiled from the files of *Science Citation Index*, a publication of the Philadelphia-based Institute for Scientific Information (ISI).

"We're very proud that a number of our prominent scientists have been recognized by their publications," said Dr. Philip S. Chen Jr., NIH associate director for intramural affairs.

Chen's work was recently lauded as well in another ISI publication, *Current Contents:* His 1956 methodology paper on microdetection of phosphorus has drawn more than 5,400 citations, making it one of the most-cited articles of all time.

Another NIH'er made the all-time list—Dr. Martin Rodbell of NIEHS. His 1964 article on the metabolism of isolated fat cells has collected more than 2,800 citations over 40 years. The SIS index covered citations of publications back to 1945.

"There are various measures of a scientist's impact," he continued. "There are prizes won, awards conferred and citations. That NIH, by virtue of having 10 highly cited scientists —and actually many more—has had this great an impact on the science of other researchers is very important."

The 10 NIH researchers found in the top 100 most-cited scientists of the decade are listed below.

Dr. Robert Gallo, chief of NCI's Laboratory of Tumor Cell Biology and co-discoverer of the HIV virus, is the world's most-cited scientist of the last decade, collecting more than 23,000 citations of his articles. His most cited paper was published in *Science* in 1984, had been cited almost 1,500 times by December 1988 and is the 10th most-cited article of the decade.

NIAID director Dr. Anthony Fauci, who is also NIH associate director for AIDS research, and chief of NIAID's Laboratory of Immunoregulation, is the eighth most-cited scientist during 1980 to 1988. He is also author of the paper most cited in the last 2 years; his review, "The human immunodeficiency virus: Infectivity and mechanisms of pathogenesis," published in a February 1988 *Science*, has already garnered more than 300 citations.

Dr. Robert C. Gallo, chief of NCI's Laboratory of Tumor Cell Biology, is the world's most-cited scientist of the last decade, collecting more than 23,000 citations of his articles.

Dr. Ira Pastan, chief of the Laboratory of Molecular Biology at NCI, has been among the top 50 most-cited researchers since 1965. For the period covering 1980 to 1988, he ranks 33rd. His most cited paper during that time is "Journey to the center of the cell: Role of the receptosome," which was published in *Science* in 1981 and collected close to 400 citations.

NCI Metabolism Branch chief Dr. Thomas Waldmann is number 34 of the top 100 most-cited scientists. His most cited paper during the 1980's is "A monoclonal antibody (anti-Tac) reactive with activated and functionally mature human T cells," which was published in the *Journal of Immunology* in 1981 and had collected 843 citations by the end of 1988. Waldmann collected almost 6,800 citations overall from 1980 to 1988.

Dr. Stuart Aaronson, chief of the Laboratory of Cellular and Molecular Biology at NCI since 1977, is the 46th most-cited scientist in the last decade. According to ISI, his 1982 *PNAS-Biology* article, "Translocation of the c-myc gene into the immunoglobulin heavy-chain locus in human Burkitt lymphoma and murine plasmacytoma cells," amassed more than 560 citations through 1988.

NCI Laboratory of Chemoprevention chief Dr. Michael Sporn was cited almost 370 times for his paper, "Transforming growth factor-b in human platelets: Identification of a major storage site, purification, and characterization," published in 1983 in the *Journal of Biological Chemistry*. He is the 51st most-cited scientist of 1980 to 1988.

Dr. William Paul, chief of the Laboratory of Immunology at NIAID, was the 53rd most-cited scientist during the 1980's, collecting close to 5,680 citations in that decade. His most-cited paper, "Identification of a T-cell derived B-cell growth factor distinct from interleukin-2," was published in a 1982 *Journal of Experimental Therapeutics*. That paper collected more than 530 citations by 1989.

NHLBI Pulmonary Branch chief Dr. Ronald Crystal, whose 1981 *American Journal of Medicine* paper, "Interstitial lung disease: current concepts of patho-

genesis, staging, and therapy," collected about 300 citations, is 59th among the 100 highly cited researchers through 1988.

Dr. John Daly, chief of the Laboratory of Bioorganic Chemistry at NIDDK and collecting more than 5,220 citations overall, ranks 62nd among the top-cited scientists.

According to *The Scientist*, his total citation count "reflects numerous high-impact papers rather than one or two blockbusters." ISI reports that at least 10 of Daly's papers have been cited more than 300 times each. His most cited paper during the 1980's was "Adenosine receptors in the central nervous system: Relationship to the central actions of methylxanthines," published in a 1981 issue of *Life Sciences*.

One other NIH researcher was recognized in ISI's top 100 top-cited scientists of the last decade—NCI Surgery Branch chief Dr. Steven Rosenberg, who wrote the 1982 *Journal of Experimental Medicine* paper, "Lymphokine-activated killer-cell phenomenon: Lysis of natural-killer resistant fresh solid tumor cells by interleukin-2 activated autologous human peripheral-blood lymphocytes," that was cited more than 680 times through 1988.

Rosenberg's true ranking could not be ascertained by ISI because another S. A. Rosenberg—Saul A., who conducts oncology research at Stanford University—was also highly cited. The Rosenbergs' papers are commingled in ISI data files. *The Scientist* estimated that articles written by NIH's S. A. Rosenberg have been cited more than 5,000 times through the 1980's.

A final interesting point noted by *The Scientist*—All ten of these highly cited scientists are career NIH'ers with 27 years average length of service.

News From and About NIHAA Members

Dr. Robert S. Bar, who was at NIH from 1974 to 1977, is currently professor of medicine, director of the division of endocrinology and director, Diabetes-Endocrinology Research Center at the University of Iowa.

Thomas G. Barbour, former assistant director for training and development, who was at NIH from 1975 to 1990, writes: "I have recently left the Public Health Service. I am teaching part-time at Montgomery College in business and management. Also, I have started a human resources management consulting company."

Dr. James A. Belli, who was a clinical associate in the Radiation Branch at NCI, has been named the initial holder of the John Sealy Centennial Chair in Radiation Therapy at the University of Texas Medical Branch, Galveston. Belli has been professor and chairman of radiation therapy there since 1982. The endowment for the named professorship was presented to UTMB by the Sealy & Smith Foundation in recognition of the 100th anniversary of the founding of John Sealy Hospital.

Dr. Glenn C. Davis, at NIMH from 1975 to 1979, is chairman in the department of psychiatry, Henry Ford Hospital, Detroit, adjunct professor of psychiatry, Case Western Reserve University School of Medicine, Cleveland, and clinical professor of psychiatry, University of Michigan School of Medicine, Ann Arbor. His current research involves risk factors for anxiety disorders and affective illness, studies of the natural history of psychiatric disorders in young adults; he currently has 2 patients at NIMH enrolled in inpatient studies.

Dr. Pierre De Meyts writes: "I was a Fogarty International postdoctoral fellow and visiting associate with Jesse Roth from January 1973 to July 1976. For the last 4 years, I was director of diabetes, endocrinology and metabolism at The City of Hope in Duarte, Calif. I am moving to Denmark on Sept. 1 as the new director of the Hagedorn Research Laboratory in Gentofte (Copenhagen), an independent basic research institute supported by Novo Nordisk."

Dr. Frank L. Douglas, NHLBI, 1979-1982, reports: "In May 1988, I was promoted to senior vice president and director of research of Ciba Geigy Pharmaceuticals. My responsibility includes discovery of new molecular entities in hypertension, angina, atherosclerosis, rheumatoid arthritis and osteoarthritis for our world wide effort."

Dr. John B. Dunbar was chief, Program Projects Branch, NHLBI, 1967-68 and a program officer, Hypertension & Kidney Diseases Branch, NHLBI, 1976-1986. Since 1986, he has been professor of epidemiology at Medical University of South Carolina, with special emphasis on health promotion for minority groups.

Drs. Emil Frei III and **Emil J Freireich,** both of whom worked together at NCI from 1955 until 1965, were presented the first of what are to be annual NIH Distinguished Alumni Awards on Sept. 10, for their considerable accomplishments in cancer treatment research. While at NCI they both developed the first successful cure for childhood cancer. They left NCI for the University of Texas M.D. Anderson

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Cancer Center and continued their research in adult leukemia. Frei became director and physician-in-chief at the Dana-Farber Cancer Institute, Boston, in 1972. Freireich stayed at M.D. Anderson, where he is professor of developmental therapeutics and medicine and director of the adult leukemia service. During 1990, he has been at NCI carrying out a special project for the NCI director. Both Frei and Freireich received small replicas of the sculpture "Healing Waters" by artist Azriel Awret, (see related story on page 5). They were also honored at a reception on Sept. 9 at the Mary Woodard Lasker Center attended by friends and colleagues.

Dr. Robert Goldberger, who was at NIH for 20 years, writes: "I left the NIH in 1981 to become provost and vice president for health sciences at Columbia University, but within a year I changed jobs, becoming provost of the entire university. Last summer, after 8 years at Columbia, I left to begin yet another career—this time in rehabilitation medicine, a field that has never really flourished. It occurred to me that I might be able to make a useful contribution if I could draw on my training as a physician, my 20 years of research experience, my administrative experience in science and higher education, and whatever insights come from being disabled myself (MS) and using a wheelchair. I am spending this year (on leave from Columbia) learning the basic medical aspects of the field at the Rusk Institute for Rehabilitation Medicine at the NYU Medical Center."

Dr. Joe R. Held, director of DRS in 1972-1984, reports that he retired from the PHS in 1984 to join the staff of the World Health Organization/Pan American Health Organization. While with WHO/PAHO, he was director of

Dr. Joe R. Held

the Pan American Zoonoses Center in Buenos Aires, Argentina, until 1987, when he was appointed coordinator of the Veterinary Public Health Program at PAHO headquarters. He recently joined the staff of Charles River Laboratories as vice-president, primate resources.

Dr. Edward A. Lichter, NIAID staff scientist 1961-66, received a Distinguished Service Award, ACPM for 1990. He is currently in the department of medicine at the University of Illinois College of Medicine.

Dr. Seymour Perry, who was at NIH from 1961 until 1980, writes that during his tenure at NIH he held various positions. From 1961 until 1974 he worked at NCI. In 1974 he was appointed special assistant to the NIH director and helped develop the NIH Consensus Development Program, becoming its first director. In 1978 he was named NIH associate director for medical applications of research and was also made acting director of the National Center for Health Care Technology, OASH. With his appointment as director and assistant surgeon general in 1980, he left NIH. Since 1982 he has been connected with Georgetown University School of Medicine where he is chairman of the department of community and family medicine and director of its Program on Technology and Health Care. He was elected to the Institute of Medicine in 1982.

Dr. Margaret Pittman, Division of Biologics Standards 1936-1971, was honored for her lifetime of scientific achievement and her contributions toward the full participation of women in microbiology with the presentation of the Alice Evans Award at a special reception during the 1990 American Society for Microbiology annual meeting.

Dr. Fred Rosen, who was at NCI as a senior assistant surgeon from 1957 until 1959, was designated "Distinguished Alumnus, 1990" during alumni reunion weekend in May at Case Western Reserve University School of Medicine. He is a 1955 graduate who is internationally known for his work in immunology and immunologic disorders and has held the Gamble Professorship at Harvard Medical School. He is also the president of Boston's Center for Blood Research and program director of the Clinical Research Center of the Children's Hospital Medical Center. During the summer, he is distinguished visiting scholar at Christ College of Cambridge University, England.

Dr. Albert Sabin, most recently at the Fogarty International Center as senior medical advisor and lecturer, delivered on Oct. 3 the fourth annual Florence Mahoney Lecture on Aging sponsored by NIA. His topic was "Aging of Individuals and of Society: Concepts, Challenges and Priorities."

Dr. Jay Skyler, a staff associate at NHLI in the Hypertension Endocrine Branch, Laboratory of Biochemical

Pharmacology from 1973 to 1975, and currently professor of medicine, pediatrics, and psychology at the University of Miami, was elected president-elect of the American Diabetes Association (ADA) during its 50th annual meeting in June 1990. He has served the ADA on the board of directors and executive committee of both the national association and the Florida affiliate, of which he was president. On the national level, he has been an active member of a variety of committees. He was founding editor-in-chief of *Diabetes Care*, a professional publication of the ADA.

Dr. George F. Vande Woude, who has been at NIH since 1972 and is currently director of the Basic Research Program at NCI's Frederick Cancer Research and Development Center, received a Robert J. and Claire Pasarow Foundation award for cancer research. The foundation, created in 1987 to stimulate medical and scientific research, also gives yearly prizes for cardiovascular and neuropsychiatry research. Each recipient receives a $35,000 cash award. The recipient's institution also receives $15,000 for support of a research fellow.

Dr. John H. Weisburger, NCI Etiology Division, 1949-1972, is now senior member, American Health Foundation, Valhalla, N.Y. He writes that he has "published over 400 research papers on the mechanism of cancer causation, with emphasis on nutrition and cancer." He recently received the Distinguished Service Award from the American Society of Preventive Oncology. He was recognized with the Ambassador award of the mid-atlantic division of the Society of Toxicology. He received a plaque from the New Jersey state commission on cancer research for leadership as chairman of the scientific review panel.

Scientists Report Gains in Understanding Alzheimer's Disease

By Bobbi Bennett

Encouraging progress is being made by intramural scientists in understanding the clinical course and genetics of Alzheimer's Disease (AD) and in designing strategies for treating it. This research was described to reporters at a recent NIH Science Writers Seminar by Dr. Stanley Rapoport, chief of NIA's Laboratory of Neurosciences; Linda E. Nee, social science analyst in the clinical neuropharmacology section, NINDS; and the seminar's moderator Dr. Trey Sunderland, chief of the Unit on Geriatric Psychopharmacology of NIMH's Laboratory of Clinical Science.

Two to 4 million Americans are believed to now suffer from AD, and experts predict that number will increase to 14 million by the middle of the next century. The dementia of this cruel disease involves memory loss, disorientation, impairment of learned skilled movements and loss of language and object-recognition abilities.

The only definitive way to diagnose AD is when an autopsy reveals large amounts of the disease's hallmarks, neuritic plaques and neurofibrillary tangles, in brain tissue. The tangles are dense networks of nerve cell fibers to which phosphate molecules have been added (phosphorylated) abnormally. The plaques are degenerating nerve cell terminals that have cores of beta-amyloid, a protein not normally found in the brain.

The plaques and tangles are not equally distributed in the AD brain. "AD is a well-behaved disease; it doesn't march indiscriminately through the brain," stated Rapoport. Rather, AD affects the association areas of the brain that process sensory inputs and are involved in higher cognitive functions such as speech, language, and elaborate planning. These regions are larger in the human brain than in that of any other mammal. AD's preference for this region has led Rapoport to theorize that the disease may have been introduced during the evolution of primates to man and may explain why there is not—and may never be—an animal model for AD.

Brain Imaging

To study the course of AD, Rapoport and his colleagues have been using PET, an *in vivo* imaging technique that can be used to measure the energy demand—and therefore metabolic activity—in regions of the human brain. They have found that, as the disease progresses, the metabolic rates decrease in the association areas. There also are differences between the corresponding association areas in the right and left hemispheres of the brain that are not seen in normal individuals. On the basis of these asymmetries, they have been able to predict, 1 to 3 years in advance, what type of deficit—language or visuo-spatial—patients with early AD will develop. For example, in right-handed patients, lower metabolic activity on the left side of the brain indicates their major problem will be with language. Such individuals will have difficulty finding the correct words when speaking but will be able to find their way home. The converse is true when the PET scan detects decreased activity on the right side. Rapoport pointed out that this predictive ability will be especially important once effective therapies are discovered because physicians could then initiate the appropriate therapy earlier.

He also mentioned a preliminary

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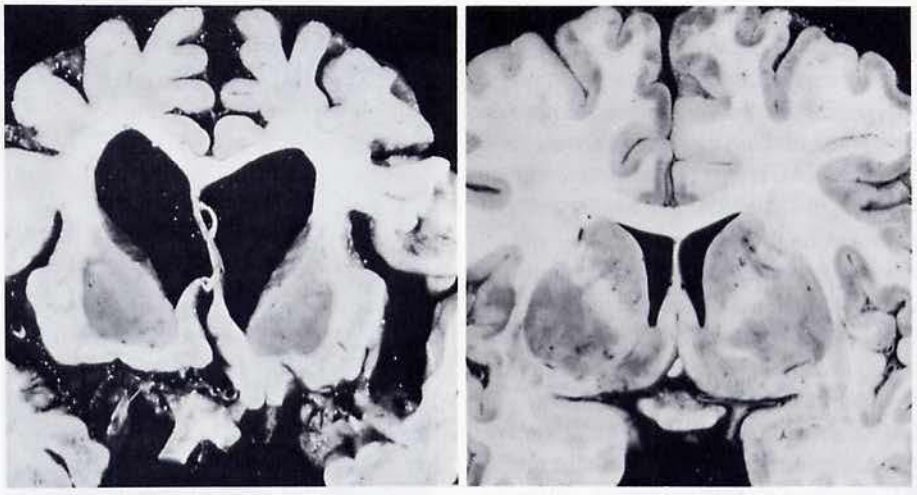
Alzheimer's (continued from p. 25)

study by members of his laboratory in which regional cerebral blood flow was measured in four AD patients with moderate dementia when their brains were "at rest" and when stimulated by a picture recognition task. The results indicated that some of their neurons in the region affected by AD were still alive and could be activated to the same extent as those of normal controls. This provides hope that when drugs are found, the brain cells of AD patients will be able to respond to them.



Patients with Alzheimer's disease lose 40 percent of their brain tissue during the 8- to 15-year course of the disease, as can be seen in the brain on the left from a 71-year-old man who died of Alzheimer's disease. The brain on the right is from a 70-year-old man who died in an automobile accident.

Genetic Heterogeneity

There are three types of AD. About 60 percent of AD cases are sporadic, that is, only one person in a family is affected. When several members of a family are affected but in a random pattern, AD is said to be familial. Patients with this type, which accounts for about 30 percent of the cases, may have a genetic predisposition to AD such as receptor sites for environmental toxins. The remainder of the cases—less than 10 percent—are of the autosomal dominant type, in which people definitely have a gene for AD that is passed from parent to offspring for at least three generations, both sexes are affected equally, and an identifiable pattern is formed. With this type, patients have an early onset, anywhere from 25 to 52 years of age.

"We've come a long way in the field of AD and in genetics," said Linda Nee, who has been trying to sort out the influence of genetic and environmental factors in AD. She has traced the disease through eight generations of a family, the largest such study ever reported. About 50 percent of the offspring were found to be affected, which indicates an autosomal dominant pattern of inheritance.

Molecular genetic analysis of this and three other large families (two of which Nee also investigated) enabled scientists in 1987 to detect a genetic marker for AD on chromosome 21. (This is the chromosome that is also involved in Down syndrome. About 50 percent of the patients with Down syndrome who live past the age of 35 develop a full-blown dementia that is indistinguishable from AD.) However, other investigators have had difficulty repeating this work. Nee believes this may be due to the heterogeneity of AD itself.

But AD is not strictly a genetic disease. In her large study of identical twins, Nee has found that both twins developed AD in only 40 percent of the pairs, a rate similar to that of identical twins catching the polio virus. In one set, a twin has had AD for 13 years yet the other remains normal. This has led her to speculate that environmental causes and more than one gene may be involved in AD.

Nee is currently following 20 families with the inherited form of AD. Their cells and pedigrees are available to other researchers through NIA's cell bank at the Coriell Institute for Medical Research in Camden, N.J.

Combination Therapy

Since 1976 when autopsied brains of patients with AD showed devastation of the cholinergic system—which uses acetylcholine (ACh) to transmit messages and is important for memory—drug research has been focused on finding ways to replace or build up the levels of ACh.

So far there has not been much success with cholinergic drugs. The most promising ones—such as physostigmine and tetrahydroaminoacridine (THA)—block the normal metabolism of ACh within the brain. But, ACh is not the only neurotransmitter or peptide that is decreased in AD. As Sunderland pointed out, "The cholinergic system takes up only a small percentage of the brain yet 40 percent of the brain is lost by the time an AD patient dies. So, other systems have to be involved." Therefore, he believes that a multiple drug approach will be needed, as in cancer chemotherapy.

Sunderland has been treating AD patients with a combination of physostigmine plus l-deprenyl. In earlier studies, his group found that low doses

of l-deprenyl produced modest cognitive and behavioral improvements in a group of 17 patients with AD. At low dosages the drug selectively inhibits the only enzyme—monoamine oxidase-B (MAO-B)—known to be elevated in AD. MAO-B is involved in the breakdown of several important neurotransmitters including dopamine, the one deficient in Parkinson's disease (PD). L-deprenyl was recently approved by the FDA for treating PD.

In the double-blind trial of the combination, 16 patients received either physostigmine plus l-deprenyl or physostigmine alone for 3 weeks, then placebo for 1 week, and then crossed over to the other drug(s) for another 3 weeks. Neither drug had any serious side effects.

This preliminary study suggests that the combination is better than physostigmine alone, but the effect appears to be additive rather than synergistic. "At this point, we'll take any improvement, given the track record of the field at large," said Sunderland.

The benefits from the combination appear to hinge on the patient's ability to achieve and maintain a high level of physostigmine in the blood. Five patients who did not achieve detectable levels of physostigmine showed no benefit from it or from the combination. The patients with the highest blood levels of physostigmine had modest improvement in memory and when they were receiving the combination therapy, these patients showed more interest in social interactions and had brighter moods. Sunderland is planning to try this combination again with twice the dosage of physostigmine and will also try other drug combinations.

Sunderland stressed, " There will not be a single magic bullet for AD therapy. Rather we envision more of a combination approach; we're attempting to build one small additive improvement on another, and hopefully get a synchronous effect that will be of even greater benefit than either drug alone."

These identical twins had autopsy-confirmed Alzheimer's disease. Twin A (l) developed the disease 2 years before her sister did, even though her sister had a history of head trauma, often thought to be a precipitating factor in AD. Identical twins were found to both develop AD only 40 percent of the time, which indicates that environmental factors probably play a role in AD.

Science Research Updates

TYPE 1 NEUROFIBROMATOSIS GENE IS IDENTIFIED

NINDS-supported scientists have reported identifying the gene that, when damaged, causes neurofibromatosis type 1 (NF1), or Von Recklinghausen neurofibromatosis, the most common nervous system disease caused by a single gene defect.

Dr. Francis Collins and colleagues at the University of Michigan, working with NINDS support, found the gene for the disorder on chromosome 17. An independent group at the University of Utah simultaneously announced the same discovery in a separate publication. (Within a month the Utah team also reported that the sequence of the gene's protein product closely resembles a protein—GTPase-activating protein, or GAP—which has been the subject of intense research because of its role, still incompletely understood, in cancer development.)

By having the gene, investigators hope to learn how the damaged gene causes NF1 and if it plays a role in some common malignancies. Ultimately, the gene discovery may result in more effective treatments such as new drugs or a replacement for a genetically altered protein.

DEFECTIVE GENE CAUSES ONE FORM OF OSTEOARTHRITIS

NIAMS-supported scientists have identified for the first time a gene that causes osteoarthritis, the most common form of arthritis. Genetic studies of three generations of a family with an unusual early developing form of osteoarthritis revealed a mutation in af-

*(See **Research Updates** p. 28)*

Research Updates
(continued from p. 27)
fected family members in the gene for collagen II, a protein that strengthens the cartilage that covers and cushions joints and that typically breaks down in osteoarthritis.

The mutation, a single base deletion, resulted in the substitution of one amino acid for another in the more than 1,000 that make up the collagen protein. The single amino acid substitution was found in all affected members of the family but not in any of the unaffected members tested or in 57 unrelated individuals.

This research lays the groundwork for identifying other mutations that may be responsible, at least in part, for many cases of osteoarthritis. Future research on such genetic mistakes may also open up new avenues for treatment. Osteoarthritis affects an estimated 16 million Americans. This work was reported by Dr. Darwin Prockop and his colleagues at Thomas Jefferson University, Philadelphia, and Dr. Roland W. Moskowitz at Case Western Reserve University in Cleveland.

RECOMBINANT PROTEIN PLUS AZT BLOCKS SPREAD OF HIV INFECTION IN HUMAN CELLS IN VITRO

Recent laboratory experiments have shown that a novel, genetically engineered therapeutic agent combining a human cell component (CD4) and a toxin (PE40) from common soil bacteria effectively kills HIV-infected human T cells and macrophages in culture, and does not harm uninfected cells. Most importantly, when the antiviral drug AZT is used together with the agent (CD4-PE40), infectious AIDS virus is eliminated from the test system.

Drs. Edward Berger, Bernard Moss and colleagues in NIAID's intramural Laboratory of Viral Diseases collaborated with Dr. Ira Pastan and his colleagues in NCI's intramural Laboratory of Molecular Biology to develop and test CD4-PE40.

CD4 is a receptor molecule, or gateway, found on the surface of some immune system cells such as T4 cells and monocyte/macrophages. An HIV surface protein called gp120 is able to attach to CD4. Once attached, the virus can use CD4 to gain entry to infect the cells, where it can replicate.

Laboratory experiments have shown that genetically engineered variants of soluble CD4, including CD4-PE40, attach to the HIV gp120 proteins found on the surface of infected cells that are producing HIV. When CD4-PE40 comes into contact with such cells, the CD4 portion attaches to the gp120 and the PE40 toxin component kills the cell.

The scientists observed that human T-cell cultures infected with HIV and then treated with a combination of CD4-PE40 plus AZT were protected from virus spread and resulting cell death. Most importantly, infected cultures treated with CD4-PE40 plus AZT showed no traces of infection with HIV even 3 weeks after removal of the drugs. In previous experiments in which similar cell cultures were exposed to HIV and not treated, all the cells died within 14 to 20 days due to spread of the virus.

While the scientists do not expect that this means they can cure an HIV-infected person, CD4-PE40 might eventually have an application in reducing the number of infected cells in a person's body and possibly slowing disease progression, particularly in combination with antiretroviral agents like AZT. Upjohn Pharmaceuticals of Kalamazoo, Michigan, has a licensing agreement with NIH to do further research on CD4-PE40.

MUTATION IN GENE INCREASES LIFE SPAN OF NEMATODE AND SLOWS ITS RATE OF AGING

An NIA-supported researcher has found that mutations in a single gene in the worm *Caenorhabditis elegans (C. elegans)* can double the maximum life span of the worm.

Dr. Thomas Johnson at the University of Colorado in Boulder reports that mutations in the worm's "age-1" gene lengthen the worm's life span, a species-specific characteristic that this research indicates is under genetic control. Scientists studying aging in animals describe senescence in terms of the rate at which age-specific mortality, or mortality at any given age, increases as the animals get older. Age-specific mortality in animals increases exponentially with age at a rate that is characteristic for each species. (Other variables that affect life span are initial mortality and high overall mortality rates for a population.) This research indicates that the rate of increase in the age-specific mortality rate is under genetic control.

Because it is a relatively simple organism and because it is well-characterized genetically, *C. elegans* provides a useful model for studying cellular processes and gene function. Additional study of the "age-1" gene may shed light on how the product of this gene can effect such a profound change in lifespan and may lead to an understanding of the role of genetics in aging in humans.

GRANTEES ESTABLISH MOLECULAR GENETIC BASIS OF ABO BLOOD GROUP SYSTEM

In work supported by NCI, scientists at the Biomembrane Institute and University of Washington, Seattle, have unraveled the molecular basis underlying the A, B, AB, and O blood groups

that are the basis of blood typing for transfusion.

Three genes, designated A, B, and O, determine blood type. As the work of these researchers now confirms, the enzymes encoded by the A and B genes convert a precursor "H" carbohydrate antigen to an A or B antigen, respectively. The O gene encodes an inactive enzyme, so the H antigen remains unaltered.

Drs. Fumi-ichiro Yamamoto, Seniitiroh Hakomori and colleagues used a probe for the A gene to screen cDNA libraries from cell lines taken from people of different blood types. They found that the gene conveying the "B" blood type is similar to the A gene except for four base substitutions. The four substitutions result in four amino acid substitutions in the encoded enzyme. The "O" gene has one base deletion in comparison with the A gene. The deletion shifts the reading frame of the DNA. As a result, the O gene encodes an entirely different and inactive enzyme.

Further study of blood group genes may offer clues to how they evolved and are evolving still. Also, the expression of the genes changes during cell differentiation and in cancer development, and study of the blood group system may provide information on these processes.

COMPUTER PROGRAM USES MOLECULAR SHAPE TO SEARCH FOR AIDS DRUGS

NIGMS grantees have developed a new technique for identifying compounds that may help treat AIDS. Using a computer program called "DOCK," Dr. Irwin Kuntz, Jr. and colleagues at the University of California-San Francisco can search the structure of a particular molecule, without preconceptions based on chemistry alone, for a shape or shapes that will fit into grooves in the molecular surface. Such grooves are usually the site of a molecule's chemical activity and, if another molecular structure can be fitted into it (rather as a key fits a lock), the activity can be blocked.

Using DOCK, Kuntz's group examined the structure (recently determined by other researchers) of a key HIV protein known as a protease. If the action of the protease is blocked, the virus cannot replicate and its infectious activity stops.

The UCSF team used DOCK to define the shape of the protease grooves. Then they searched for compounds with that shape by using a database containing the structures of 60,000 molecules. The database identified haloperidol, a common antipsychotic drug, as a possible fit for the protease groove. Unfortunately, haloperidol is not effective against HIV unless the drug is used in doses that greatly exceed the lethal limits for human beings. For this reason, haloperidol is only a starting point for Kuntz and other UCSF researchers in their efforts to use the techniques of structural biology to design anti-AIDS drugs. The scientists are now making changes in haloperidol's structure that they hope will preserve the desired activity while lessening toxicity.

TRANSGENIC MICE PRODUCE SICKLE HEMOGLOBIN; MAY PROVIDE ANIMAL MODEL OF SICKLE CELL DISEASE

NIH grantees have made transgenic mice that produce human sickle hemoglobin. Scientists supported by NHLBI, NICHD, and NCI—Drs. Thomas M. Ryan and Tim M. Townes at the University of Alabama at Birmingham, Drs. Toshio Asakura and Ralph L. Brinster at the University of Pennsylvania, Philadelphia, and Dr. Richard D. Palmiter at the University of Washington, Seattle—injected human genes for sickle hemoglobin into fertilized mouse eggs. The mice that had incorporated the human genes—and that as a result made human sickle hemoglobin—were crossed with mice that had beta thalassemia, a form of anemia which impairs the animals' ability to make normal mouse hemoglobin. With levels of mouse hemoglobin in the hybrid mice reduced, most of the red blood cells of the hybrid mice became sickled when the oxygen supply was lowered. The animals developed signs of moderate anemia, but not as severe as seen in patients with sickle cell disease.

The transgenic mice developed in this research are the closest approach to date to an animal model of sickle cell. Studies are under way to determine whether these animals develop the tissue and organ damage characteristic of sickle cell disease. The mice will be an important tool for studying the effects of sickle cell anemia and for evaluating new treatments.

This material was compiled by Charlotte Armstrong, Office of Communications, OD.

Executive Director Sought for NIHAA

The NIHAA is seeking an executive director to direct its day-to-day operations. Responsibilities include financial management, fund raising and membership. NIH scientific/administrative experience desirable. Call Cal Baldwin (301) 949-1697. Harriet Greenwald, current executive director, will continue as Editor of *NIHAA Update.*

Stetten *(continued from p. 1)*

In 1934, Stetten took his M.D. degree at the College of Physicians and Surgeons of Columbia University, after which he did his internship and residency at Bellevue Hospital in New York City. There he first encountered another NIH luminary, James A. Shannon, who enjoyed a reputation as something of a genius as a visiting physician on Bellevue's renal service. Stetten returned to Columbia to take a Ph.D. in biochemistry under Rudolf Schoenheimer in 1940. At this time very little was known about the fate of particular atoms and larger molecular parts of various metabolites in terms of interconversion with other types of substances in the animal body. Stetten pioneered with Schoenheimer in utilizing the stable, heavy isotopes of nitrogen and hydrogen N^{15} and D to demonstrate the dynamic relationship between molecules of various fatty acids and cholesterol, choline and ethanolamine, choline and phosphatides, glycogen and galactose, and inositol and glucose. His dissertation research, which was published as two papers in the *Journal of Biological Chemistry*, utilized the then-new technique of labeling isotopes and examined the biological interconversion of fatty acids. The following year he married a fellow graduate student, Marjorie Roloff, known as "Marney," thus launching a scientific and domestic partnership that spanned more than four decades, until her death in 1983.

From 1938 to 1947, Stetten taught biochemistry at Columbia University, after which he moved for 1 year to Harvard University. The war years brought a variety of students to Columbia. One of these was Juan Salcedo, who later eliminated the nutritional disease beri beri from Bataan province and went on to hold numerous high scientific offices in the Philippines. At Harvard, Gordon Tomkins, who later became chief of the Laboratory of Molecular Biology, NIAMD, enrolled in Stetten's course on the clinical aspects of biochemistry, a decision that contributed to Tomkins's decision to make a career in biochemistry.

From 1948 to 1954, Stetten served as chief of the division of nutrition and physiology of the Public Health Research Institute of the City of New York, a period he described as one of the most productive of his life. His laboratory also attracted a number of postdoctoral fellows, including another future NIH director, James Wyngaarden.

Dr. James B. Wyngaarden (l) poses with Dr. DeWitt Stetten Jr. when Stetten retired officially on Jan. 1, 1986, and was named NIH deputy director for science, emeritus.

Among his achievements during this period, Stetten elucidated the physiology of gout, showing that patients with gout produce abnormally large amounts of uric acid, the accumulation of which is the cause of all clinical physical difficulty. For his research during this period, Stetten was honored with election to the National Academy of Sciences.

In 1954, Stetten came to NIH as associate director in charge of research at what was then called the National Institute of Arthritis and Metabolic Diseases (NIAMD). He served in this capacity until 1962. During this period he was coauthor on early editions of a standard textbook, *Principles of Biochemistry*. As NIAMD intramural director, Stetten recruited a number of young scientists to Bethesda, including the intramural program's first Nobel laureate, Dr. Marshall W. Nirenberg. Dr. Joseph E. Rall was not only recruited by Stetten but also stayed to follow in his mentor's footsteps, first as intramural director of NIAMD and later as NIH deputy director for science. During this period, Stetten also contributed to the establishment of the Foundation for Advanced Education in the Sciences, Inc., and later served as its president.

From 1962 until 1970, Stetten served as first dean of the Rutgers University Medical School, returning to NIH in 1970 as director of the National Institute of General Medical Sciences. Among the programs sponsored by NIGMS during his tenure were the Medical Scientist Training Program, which underwrote the educational costs of M.D.-Ph.D. students who planned to make a career in research, and the establishment of eight genetics centers across the nation, which maintained a bank of cell lines representing genetic defects and sponsored basic and clinical programs for the identification of genetically transmitted diseases.

In 1974, Stetten assumed the position of NIH deputy director for science. He served during this time as chairman of the recombinant DNA advisory committee. In response to concern within the scientific community about potential dangers in biotechnology research, this committee drafted guidelines for scientists using the new techniques. One drawback to moving to Bldg. 1, Stetten always believed, was that the scientific director often found himself isolated from the research he hoped to foster. To counter this, he established a Friday morning seminar series devoted

exclusively to the presentation of laboratory and clinical research activities.

In 1978, Stetten asked to be relieved of his duties as deputy director because of deteriorating eyesight caused by macular degeneration, and Dr. Donald Fredrickson, then NIH director, appointed him senior scientific advisor to the director. From an office in Stone House, Stetten took up a number of new projects. He wrote a widely cited letter to the editor of the *New England Journal of Medicine* suggesting that ophthalmologists learn more about advising their visually handicapped patients on services available for the blind. Some years later, the Library of Congress recognized his efforts on behalf of blind and low vision people by asking him to pose for a poster promoting its Talking Books program.

In another project, undertaken with William T. Carrigan, Stetten edited a book on the NIH intramural program, *NIH: An Account of Research in Its Laboratories and Clinics*. He also founded the Museum of Medical Research at NIH, which was established during the NIH Centennial observance and which bears his name. In the museum's collection is a gavel made by Stetten for NIH Director Robert Q. Marston and passed to his successors. An avid woodworker, Stetten had made the gavel on his own lathe. For the head he used wood from the plane tree found on the Aegean island of Cos and associated with Hippocrates, the father of medicine. The handle was made of American cherry wood. Among his many awards and honors were the Banting Medal from the American Diabetes Association, DHEW Superior Service and Distinguished Service awards, honorary doctorates from Washington University and from the College of Medicine and Dentistry of New Jersey, and the presidency of the Society for Experimental Biology and Medicine.

"To me, Hans was the epitome of the modern biomedical leader who embodies excellence in scholarship, in academic teaching skills and administrative acumen, and in humanistic sensitivity," said Dr. Philip S. Chen Jr., NIH associate director for intramural affairs.

"I think his heart really lay with the intramural part of NIH," Chen continued. "He leaped at the chance to become deputy director for science in 1974 when (then director) Bob Stone offered him the job. He had been a scientific director at the arthritis institute and this post allowed him to maintain a close finger on the pulse of the scientific directors.

"It was at this time that he instituted the Friday morning seminars, which were an honored forum for scientists to tell about their work. He continued that tradition even after he stepped down in 1979." The last of the seminars was held June 1, 1990.

"To me, Hans was the epitome of the modern biomedical leader who embodies excellence in scholarship, in academic teaching skills and administrative acumen, and in humanistic sensitivity."

–Dr. Philip S. Chen Jr.

Bobbi Bennett, NIH special assistant for scientific information, attended those sessions regularly.

"I was privileged to attend Dr. Stetten's weekly seminars for 10 years and hear the best and brightest intramural scientists describe their research," she said. "It was a fantastic education. Dr. Stetten considered these seminars the best part of his week, and so did I. The speakers came because of their respect for him.

"Dr. Stetten combined brilliance with compassion and gentleness," Bennett concluded. "He was the ideal physician, scientist, teacher and human being."

Commented Dr. Joseph E. Rall, NIH deputy director for intramural research, "Dr. Stetten hired me 35 years ago and has been mentor, friend and colleague ever since. Hans Stetten has been the paradigm of distinguished scholarship and humanitarianism. The NIH has benefitted from his wisdom and insight for over three decades and we shall miss him deeply."

Regarding Stetten's nickname, Chen explained: "The name Hans originated with a German housekeeper that the Stetten family had for many years. She called him Hansel and called his sister Gretel. The name stuck."

Concluded Chen, "He had a very broad knowledge of science generally, and an encyclopedic knowledge of biomedical areas. Basically he was a very highly respected, approachable, wise person. His counsel was widely sought. And accepted."

Stetten is survived by his wife, Jane Lazarow Stetten; four children of his first marriage: Dr. Gail Stetten of Baltimore, Dr. Nancy Stetten of Nashville, Mary Stetten Carson of New York City, and George Stetten of Syracuse, N.Y.; two stepsons: Dr. Paul Lazarow and Dr. Normand Lazarow; and eight grandchildren: Elizabeth and Alex Maloney, Anna and Joseph Einstein, Magdalin and Matthew Carson, and Amy and Wendy Stetten.

A memorial service was held Oct. 29 in Lipsett Amphitheater, Bldg. 10.

Gene Therapy *(continued from p. 1)*

About two ounces of the patient's own genetically repaired cells, suspended in saline solution, were reinfused intravenously to the patient—a 4-year-old girl diagnosed with adenosine deaminase (ADA) deficiency.

ADA deficiency is a rare, genetic disease that severely cripples the immune system, leaving patients vulnerable to serious infections. Less than 10 children a year in North America are born with the disease, which often results in death in the first years of life.

The patient was awake and mobile during the treatment, which took about 30 minutes. The therapy is the first of several periodic treatments the patient will have in the next 6 months to a year. Eventually, NIH researchers hope patients will be able to receive the gene treatments at their home hospitals.

No outward physical results of the treatment are expected to be evident for several months; however, periodic blood samples from the patient will measure the amount of repaired cells circulating in the patient's body and will give researchers a wide representation of what infections the blood cells have to fight against during a typical year.

"We would hope that we'll begin seeing effects of the gene's modified cells in the first year," said Blaese, who has made his career taking care of children with severe immune disorders.

"I certainly don't expect to tell you next week that this treatment is a roaring success," he cautioned. "It's not designed to give answers within a week. It's designed to help us for a long period of time."

"We really feel a very large burden on our shoulders," Anderson said, answering questions at a press conference held the day before the treatment was scheduled.

One reporter asked him why the investigators decided to infuse so few "corrected gene" cells. Wouldn't more cells have produced a greater impact on the experiment? the journalist wanted to know.

Announcing the gene therapy trial at a press conference on Sept. 13 are (from l) Dr. R. Michael Blaese, NCI, Dr. W. French Anderson, NHLBI, and Dr. Kenneth Culver, NCI.

"There have been critics who have said 'Why are you starting so soon?' and why are we going with a child?" Anderson answered. "It is imperative that we not do anything wrong or dumb or have it go badly."

He continued: "Our point of view is, it is more important to start very slowly so that we are ultrasafe than to move quickly ahead and than take the chance that something we did not anticipate would happen."

Put in perspective, the amount of cells reintroduced to the patient does seem small.

About 1 billion human cells—a tiny fraction of the body's total cells—were involved in this first stage of the trial, according to the third principal investigator, Dr. Kenneth Culver, a senior clinical researcher in Blaese's section.

"A drop in the bucket," he said smiling, as Anderson indicated with his thumb and forefinger the pellet-size amount of history being discussed.

Of course, the implications of the trial, much grander and more far-reaching than the tiny pellet of cells would indicate, were not considered lightly by the researchers.

"The technical ability to do gene therapy has been around for several years," Anderson said, addressing the ethical issue—sometimes called "the Frankenstein concern"—posed by critics since gene therapy technology was initiated some 20 years ago.

He explained: "The concern has been that as soon as scientists and physicians, no matter how dedicated and how conscientious, begin to manipulate and engineer the blueprint of our lives—our genes, that concept is very disturbing."

Even during the press conference, one group of critics was silently making its concerns known.

Press releases from the Foundation on Economic Trends, a Washington D.C., think-tank, were neatly stacked beside gene therapy fact sheets on a table just outside the Bldg. 31A conference room where trial investigators fielded media questions.

"The NIH has brought us into the Brave New World of human genetic engineering," Jeremy Rifkin, foundation president, said in the release. "We are calling for a complete halt on future human gene therapy experiments until an advisory board on eugenics is established that will fully assess each proposed experiment.

"While there are many potential benefits of somatic gene therapy," Rifkin continued, "the technology has the potential of being misused and abused on a massive scale. The social and ethical impacts of human genetic engineering may be the most profound ever to

face humanity. They cannot be ignored by the NIH." Far from ignoring the ethical impact of the trial, Anderson recounted the numerous tests gene therapy in general, and this trial specifically, have had to pass before arriving at September's threshold of discovery.

"The review process was set up to give the public confidence that when gene therapy was finally attempted, it would not take place in some haphazard or random or rushed way," he said. "It was thoroughly reviewed over a long period of time by a large number of committees composed of very conscientious people who were looking for any possible problem.

"The reason it's taken us over 3 years to get approval is that a large number of people have done a very dedicated job," he said.

Anderson also emphasized the importance of animal research to the development of the gene therapy trial.

"Our goal is to devise treatment for incurable human diseases," he said. "Research with animals is critical for the success of that objective."

Anderson said the extensive approval process helped the public understand the importance and safety of the trial.

"I think the American public, from my interactions and from talking with groups, are comfortable and as excited as we are," he said. "What we hope for is that the procedure goes well and that this child and other children are ultimately helped."

What began in September in the arm of a 4-year-old could ultimately eliminate the world's most serious and devastating disorders, according to Anderson.

"The longer term implication, if this works, is that gene therapy might very well become a major new revolution in medicine," Anderson concluded. "This should provide cures for what are presently incurable diseases."

Why the Office of Scientific Integrity?

By Dr. Jules V. Hallum and Dr. Suzanne W. Hadley

It is a pleasure for us to introduce the Office of Scientific Integrity (OSI) to the members of the NIHAA. The OSI is a relatively new office, established in April 1989. In establishing the OSI, the PHS was expressing its concern for maintaining the high regard in which the American biomedical research enterprise had been traditionally held by the public. A few highly publicized cases of scientific misconduct were seen to have been damaging to the reputation of science. In an attempt to raise the public's perception of science and scientists, new research regulations were promulgated, taking into account the input of the scientific community. These research regulations, the so-called "Final Rule," contain several significant elements, three of which are important to this discussion.

The rule defines scientific misconduct as "fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the scientific community for proposing, conducting or reporting research." Specifically, misconduct does not include honest error or honest differences in interpretations or judgements of data.

The rule establishes the OSI and the Office of Scientific Integrity Review (OSIR) as two independent but complementary elements of the PHS effort for dealing with alleged and confirmed scientific misconduct.

The rule requires that any institution applying for or receiving PHS funds for research have in place policies and procedures, developed by the institution itself, to deal with alleged or suspected scientific misconduct. Institutions are required to submit an annual assurance to the OSI about their compliance with this aspect of the Final Rule.

The OSI is best described by its responsibilities. It was established within NIH, but has PHS-wide authority, including CDC, FDA, HRSA, ADAMHA and NIH for both intra- and extramural research. The OSI has four major duties:

1. The OSI oversees implementation of all policies and procedures related to matters of possible scientific misconduct.

2. The OSI oversees each investigation into alleged or suspected scientific misconduct conducted by any institution applying for or receiving PHS research funds.

3. The OSI conducts inquiries or investigations, when necessary.

4. The OSI also participates in and directs preventive and educational measures to encourage the responsible conduct of research. As examples of this activity, the OSI is conducting a workshop for biomedical journal editors to determine ways in which the editors can interact with the OSI in matters related to suspected misconduct in scientific publications. In addition, a series of regional meetings are to be held this coming spring with institutional representatives to determine the institutions' experiences during the first year of implementation of the Final Rule.

How does the OSI work in cases of alleged scientific misconduct? Institutions are required to notify the OSI when, after an initial inquiry or fact-finding phase, a formal investigation will be undertaken. The OSI follows the investigation for thoroughness, fairness, objectivity and timeliness. Upon conclusion of the investigation, the OSI receives a full report on the institution's investigation citing the evidence, findings, and conclusions, and sanctions imposed, if any. The OSI reviews the

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Integrity *(continued from p. 33)*
report and decides if the findings of the investigation are fair and consistent with the evidence. If misconduct is confirmed, and the OSI agrees, the report is forwarded, together with any additional sanctions imposed by the OSI, to the appropriate agency director who then sends it to the OSIR for review. The OSIR, if it approves, sends the report to the Assistant Secretary for Health (ASH) for further review and decision.

If the OSI does not accept the findings of an institution's investigation, it can ask that the institution reopen the investigation, or the OSI can open its own inquiry or investigation.

The OSI can also open an inquiry or investigation following allegations made directly to the office. If an inquiry shows no evidence to warrant a formal investigation, the case can be closed at that time. If the inquiry demonstrates that there are facts to support an allegation that misconduct may have occurred, a formal investigation is initiated. The investigation is not simply an extended inquiry, but a formal process to determine if scientific misconduct did occur, and if so, how serious it was, and who was responsible. The same process is used within the PHS for allegations of scientific misconduct in extramural research.

In both inquiries and investigations, the OSI is specifically charged with protecting the rights of the complainant and the reputation of the respondent. It does this in two ways. First, all of the deliberations and reports of the OSI are kept in the strictest confidence. Only when a finding of misconduct is proved and sanctions are approved by the ASH does the final report become available to the public.

If the respondent is found not to have committed an act of misconduct, the OSI offers a choice. The final report can be kept confidential, secure from release under the Freedom of Information Act, or, if the respondent wishes, perhaps because of media publicity, the OSI will work to help clear the respondent's reputation.

Most of us would like to believe that instances of scientific misconduct are rare, indeed. Whether or not this is true, it is recognized that even one case can have dramatic and costly impacts. At the present time, OSI is dealing with approximately 80 active cases. It has resolved 75 in the past 18 months. By resolving these cases in a thorough, fair and professional way, the OSI believes that it is participating as a partner in the scientific dialogue. That all of the members of the OSI professional staff are themselves scientists indicates the commitment of OSI in participating in this dialogue.

Scientists must recognize that they are in partnership with the OSI, sharing the responsibility for protecting PHS research funds. Universities must also share in this responsibility, because of their position as leading producers of both scientific research and researchers. The universities' responsibility to inculcate students in responsible research practices is a particularly crucial responsibility.

If partnership between the scientific community, the institutes and universities and the OSI is properly forged and maintained, it will provide a demonstration that science can indeed govern itself and thus help us to reestablish the high regard of science by the public and its representatives. The OSI is committed to this partnership.

Dr. Hallum is director of the Office of Scientific Integrity and Dr. Hadley is deputy director.

NIH Notes for June—October 1990

HONORS AND AWARDS

Dr. Samuel Broder, NCI director, received the Health Leader of the Year Award from the Commissioned Officers Association of the U.S.P.H.S. "in recognition of his outstanding contributions to the development of new treatments for both cancer and AIDS, through which he has touched and extended the lives of people throughout the world" ... **Dr. C. Marius Clore** of NIDDK's Laboratory of Chemical Physics was named 1990 Distinguished Young Scientist by the Maryland Science Center ... **Dr. Lois K. Cohen**, extramural program director at NIDR, was a special guest speaker at the University of Florida College of Dentistry when it dedicated the NIDR-supported Claude Pepper Center for Research on Oral Health in Aging ... **David S. Dwyer**, a management analyst in DRG, was named one of America's "thousand points of light" by President George Bush for his volunteer work as chief of the Bethesda-Chevy Chase Rescue Squad. Dwyer was also honored, a week later, as the recipient of one of 12 Volunteer Administrator Awards for 1990 from Governor Schaefer of Maryland ... **Dr. Anthony S. Fauci,** NIAID director, received honorary degrees from four educational institutions. The degree of doctor of science, honoris causa, was conferred on him during graduation ceremonies at Mount Sinai Medical Center, New York City; Georgetown University School of Medicine; Neumann College, Aston, Pa.; and Hahnemann University, Philadelphia, where he also delivered the commencement address to the graduate school and school of medicine. In addition, he delivered the commencement address to the Harvard Medical School class of 1990 ... **Dr. Carolyn A. Felix**, a biotechnology fellow in NCI's Pediatrics Branch, was the 1990 recipient of the American Society of Pediatric Hematology/Oncology's Young Investigator Award for her work in molecular genetics of lymphoblastic leukemia ... **Dr. Michael M. Frank**, NIAID's clinical director and chief of NIAID's Laboratory of Clinical Investigation, delivered the 1990 Jerome Glaser Memorial Lectureship on "Complement and Disease" at the annual meeting of the American Academy of Allergy and Immunology ... **Dr. George J. Galasso,** NIH

associate director for extramural affairs, was voted president-elect of the International Antiviral Research Society at its annual meeting in Brussels. This recognizes his longstanding involvement in antiviral research ... **Dr. Robert C. Gallo,** chief of NCI's Laboratory of Tumor Cell Biology, was one of eight scientists honored for outstanding achievements in laboratory science by the American Association for Clinical Chemistry. He was cited for pioneering the field of retrovirology and for discovering T-cell growth factor, or interleukin-2 ... **Dr. Igal Gery,** chief of the experimental immunology section, Laboratory of Immunology, NEI, received an unsolicited and unrestricted award of $50,000 from the Alcon Research Institute to use in a research project ... **Dr. Ada Sue Hinshaw,** director of NIH's National Center for Nursing Research, was awarded an honorary doctor of science degree from Marquette University in Milwaukee. She was honored for emphasizing the work of nurse researchers and helping to shape the direction of the nation's health care policies ... **Dr. Arthur Jacobson,** an organic chemist in NIDDK's Laboratory of Medicinal Chemistry, was chosen for the J. Michael Morrison Award for outstanding contributions in scientific administration related to drugs of abuse ... **Dr. Michael A. Kaliner,** head of the allergic diseases section of the Laboratory of Clinical Investigation, NIAID, delivered the 18th Annual Clemens von Pirquet Lecture at Georgetown Medical Center. His theme was "Asthma in the 1990s: Translation of Pathogenetic Studies into New Therapeutic Strategies." He also received the Clemens von Pirquet Award for significant contributions to the field of allergy and clinical immunology ... **Dr. Ruth L. Kirschstein,** NIGMS director, received the 1990 Dr. Nathan Davis Award from the American Medical Association in recognition of her distinguished 34-year federal career as a researcher, manager and executive ... **Dr. Donald A. B. Lindberg,** director of NLM, was awarded an honorary doctor of laws degree from the University of Missouri at Columbia ... **Dr. Harald Löe,** director of NIDR, received an honorary doctor of humane letters from the University of South Carolina for his "accomplishments and dedication to excellence in education, research, and patient care in the field of dental medicine" ... **Dr. Karin Nelson,** a pediatric neurologist in the Neuroepidemiology Branch of NINDS, received the Weinstein-Goldenson Research Award given by the United Cerebral Palsy Association for "opening up a new chapter in the epidemiology of cerebral palsy and other developmental disabilities" ... **Caroline Percopo** of NEI's immunology and virology section, Laboratory of Immunology, is one of five recipients of the 1990 Raymond W. Sarber Fellowship Award, granted to students for their exceptional research ... **Dr. Steven A. Rosenberg,** chief of NCI's Surgery Branch, was named 1990 Scientist of the Year by *R&D Magazine*, an international research and development publication, for his "distinguished work in adoptive immunotherapy and overall contribution to science and the advancement of knowledge" ... **Dr. Novera Herbert Spector,** health scientist administrator in the Division of Fundamental Neurosciences, NINDS, has been awarded the first Sergei Metalnikoff gold medal by the International Society for Neuroimmunomodulation (ISNIM). He was cited for his service as first president of ISNIM, for his outstanding research, and for his numerous seminal ideas leading to an explosion of new fundamental research in neuroimmunomodulation (NIM) ... **Dr. Earl R. Stadtman and Dr. Thressa C. Stadtman,** both members of the Laboratory of Biochemistry, NHLBI, were honored at a symposium in New Orleans on June 3. Each turned 70 this year and the alumni of their laboratory took the opportunity of celebrating their milestones by organizing a symposium entitled "Cellular Regulation" as part of the annual meeting of the American Society for Biochemistry and Molecular Biology and the American Association of Immunologists. They were two of the founding members of the intramural staff of the then National Heart Institute, arriving at NIH in Fall 1950. They are the only founding members of NHI still active at the bench at NIH ... **Dr. Stephen M. Weiss**, chief of NHLBI's Behavioral Branch, has been elected president of the International Society of Behavioral Medicine. He was president of the U.S. Society of Behavioral Medicine from 1984 to 1985.

APPOINTMENTS AND PERSONNEL CHANGES

Dr. Richard H. Adamson, director of NCI's Division of Cancer Etiology, has been appointed acting deputy director of NCI ... **Dr. Neil Buckholtz,** formerly executive secretary of the behavioral neurobiology study section in the Division of Extramural Activities, NIMH, has been named a health scientist administrator for the Neuroscience and Neuropsychology of Aging Program. He will direct the treatment and management section of the Dementias of Aging Branch, which includes clinical trials of pharmacological agents in Alzheimer's disease and studies of behavioral and environmental interactions ... **Lucretia "Chris" Coffer,** who has worked in the federal government for 26 years with a background of EEO assignments, has joined the Division of Equal Opportunity and will serve as the Federal Women's Program manager. Her chief responsibilities will be directing, developing and evaluating NIH's Federal Women's Program. She will focus on matters pertaining to the employment stance of more than 6,000 women at NIH by developing policies and reviewing current practices affecting the employment of women ... **Dr. Marlene Cole** was appointed deputy director for operations of the Veterinary Resources Program, National Center for Research Resources ... **Dr. Janet M. Cuca** has been named NEI review and special projects officer, extramural collaborative programs ... **Dr. John W. Diggs,** director of the Division of Extramural Activities at NIAID since 1982, has been named NIH deputy director for extramural research, a position formerly held by Dr. Katherine Bick, who left NIH for private industry last March. In his new position, Diggs will direct the development and implementation of NIH policies and procedures for awarding funds for biomedical research and provide policy guidance for NIH components that make grants and contracts. The responsibilities of the Office of Extramural Research also include human subjects protection, animal welfare, research training policies, institutional liaison, invention reporting and coordination of research funding for small businesses ... **James Doherty,** information officer for DRS since 1982, has been chosen public affairs officer of NCRR, heading the Office of Science and Health Reports. NCRR was formed by a merger of the Division of Research Resources and Division of Research Services ... **Dr. Margaret Holmes,** who has been acting chief of NCI's Cancer Centers Branch, has been named the branch's permanent chief. She has been with the centers program since 1984 and at NCI since 1978 ... **Dr. Eric Juengst,** a philosopher specializing in the ethical dilemmas that can arise with advances in medical technology, has joined the National Center for Human

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Genome Research (NCHGR) to direct its efforts to anticipate the ethical, legal and social implications of human genome research. He comes to NCHGR from Pennsylvania State University college of medicine, where he was assistant professor of philosophy in the department of humanities ... **Dr. Rochelle M. Long,** an assistant professor in the department of pharmacology and toxicology in the school of pharmacy at the University of Maryland, has been named a program administrator in NIGMS' Pharmacological Sciences Program. She will handle research grants and predoctoral training grants in the area of pharmacology ... **Dr. Ernest Marquez** has joined the NIGMS Office of Review Activities as an executive secretary of the Minority Biomedical Research Support review subcommittee. He comes to NIGMS from Cambridge BioScience Corp., where he directed microbiology product development ... **Dr. Thomas D. Mays** has been named acting director of NCI's Office of Technology Development, which oversees legislation, rules, regulations related to NCI Cooperative Research and Development Agreements, employee invention reports, patents, licensing, and royalty income. Before coming to NCI, he was a primary patent examiner with the U.S. Patent and Trademark Office ... **Martha Pine,** NIGMS deputy executive officer since 1981, has been appointed executive officer for the institute. She identifies the institute's minority biomedical research and training programs as one of the areas she plans to emphasize over the next few years ... **Perry S. Plexico** has been named chief of the Computer Systems Laboratory (CSL), DCRT. CSL is the engineering arm of DCRT and Plexico is an electronics engineer. He came to DCRT in 1962 and since 1969 has been involved with CSL ... **Dr. Louise E. Ramm** has been appointed director of the Biological Models and Materials Program at NCRR ...**Dr. Michael Rogers** has been named deputy director of NIGMS' Pharmacological Science Program. In addition to his new position, he will continue to oversee grants involving bio-related chemistry ... **Dr. Stephen M. Rose** has been selected chief of the Genetics and Transplantation Branch of NIAID's Division of Allergy, Immunology, and Transplantation. He previously held the position of assistant professor, department of cell biology, at the University of New Mexico Cancer Research Center. His field of expertise is molecular immunology and immunogenetics and his research focused on how chromatin structure affects the activation of immunoglobulin genes ... **Dr. John Ruffin,** dean of the college of arts and sciences and professor of biology at North Carolina Central University, Durham, has been named to the newly established position of NIH associate director for minority programs. In his new position, he will have overall responsibility for development and coordination of NIH activities to strengthen minority research and training programs, improve the effectiveness of all programs aimed at increasing minority participation in biomedical research, foster research related specifically to minority health issues, enhance the research capabilities of predominantly minority institutions and ensure effective participation of the extramural and intramural scientific communities in these matters ... **Kathy L. Russell,** deputy administrative officer in NCI's Division of Cancer Treatment, has left for her new post at Georgetown University, where she will work for NCI alumnus Dr. Marc Lippman. She will remain president of the board of directors of the Children's Inn at NIH ... **Dr. Gisele Sarosy** has been named chief of the International Cancer Research Databank Branch of NCI ... **Dr. Walter Schaffer** has joined the Office of Extramural Research, OD, to serve as research training and research resources officer ... **Dr. Mary Ann Sestili,** formerly the executive director of the Linda Pollin Foundation, and prior to that holder of positions in both program and review areas at NCI, has been appointed director of the Office of Review at NCRR ... **Dr. Charles R. Sherman,** assistant chief of the Planning and Policy Research Branch within the Office of Science Policy and Legislation, OD, has been named deputy director of the Office of Medical Applications of Research, OD. He will focus his efforts on evaluating the impact and overall effectiveness of the office's programs, including its consensus development conferences ... **Dr. Edward J. Sondik** has been appointed deputy director of NCI's Division of Cancer Prevention and Control. He had been serving as acting deputy director since September 1989. Earlier Sondik was associate director of the division's Surveillance Program ... **Dr. Peter Steinert** has been chosen to direct a new intramural laboratory at NIAMS to carry out basic research on the skin. The new Laboratory of Skin Biology will conduct fundamental studies that explore the nature and function of proteins responsible for the maturation of the epidermis, the skin's outermost layer. From 1973 until 1989, when he joined NIAMS, Steinert worked in the Dermatology Branch of NCI ... **Dr. Mary Jane Stephens** has joined the NIGMS Office of Review Activities as executive secretary of the Minority Biomedical Research Support review subcommittee. She comes to NIGMS from the Food and Drug Administration, where she served as a senior staff fellow in the division of microbiology ... **Carol Tippery** has been appointed NIGMS grants management officer. In this position, she will be responsible for the financial management aspects of all research and training grants assigned to NIGMS. Associated with NIH since 1963, she has previously worked for DRG, NICHD and NIA, where she was grants management officer from 1987 to 1990 ...**Dr. Jose Velazquez,** formerly chairman of the department of anatomy and cell biology at the Universidad Central del Caribe School of Medicine in Cayay, Puerto Rico, has joined the Minority Biomedical Research Support Program at NIGMS ... **Dr. Lorrita Watson** has become a program administrator in the MBRS Program at NIGMS ... **Dr. Lon White,** chief of the Epidemiology, Demography and Biometry Program, NIA, will now head the newly established Asia-Pacific office in Honolulu to coordinate NIA's epidemiological research activities in Hawaii, the Pacific and Asia ... **Theresa Wilson** has left NIH after more than 31 years to accept a position as a scientific reviewer with the FDA. She began her federal service at NIH in the Clinical Center's clinical pathology department in Oct. 1958, as a medical technologist in the clinical chemistry service. In 1959, she became the supervisor of what is now known as the general chemistry group and later became involved in electrophoresis method development and evaluation. From that time to the present, she was supervisor of the electrophoresis group ... **Dr. Robert E. Wittes** is returning to NCI to become chief of the Medicine Branch at NCI's Division of Cancer Treatment. He had been vice president for cancer research at Bristol-Myers Squibb. He joined the company in 1988. Prior to that he had been director of NCI's Cancer Therapy Evaluation Program from 1983 until 1988 ... **Dr. David A. Wolff,** formerly deputy associate director for program activities, NIGMS, has been appointed to head the Fogarty International Center's International Research and Awards' Branch. This branch is responsible for the manage-

ment of a number of research and research training programs, including international research fellowships for foreign scientists to conduct research at U.S. institutions, and senior international fellowships for senior U.S. scientists conducting collaboration research abroad. Wolff joined the NIH Grants Associates Program in 1978, and held a position at NIDR before joining NIGMS ... **Dr. Marian Zatz** has been appointed chief of the cellular basis of disease section of the NIGMS Cellular and Molecular Basis of Disease Program. She had been a program administrator in the section since 1984.

RETIREMENTS

Dr. Robert L. Bowman, chief of NHLBI's Laboratory of Technical Development, retired on June 1. He joined NHLBI in June 1950 as a senior assistant surgeon in the Laboratory of Technical Development (LTD). In 1956 he was named chief of LTD, a post he held until he retired. Among the best known instruments developed by Bowman was the spectrophotofluorometer. It enabled investigators to use fluorescent techniques in the study of biological compounds. An example is the work on neurotransmitters by Dr. Julius Axelrod, who utilized Bowman's instrument to do the work for which he won the Nobel Prize ...

Dr. David P. Rall (l) holds up poster signed by hundreds of NIEHS employees thanking him for his years of leadership as NIEHS director. Presenting the poster on behalf of the employees is Dr. David G. Hoel, acting director, NIEHS.

Robert L. Bunch, a supply technician and property manager at NIDR, retired after 36 years of government service, the last 27 of them with NIDR. He began working at NIH in 1953, and since then has held a variety of jobs ordering and cataloguing supplies and equipment. His retirement plans include a lot of fishing and he may expand his interest in sports into a second career by opening a sporting goods shop ... **Marjorie Price Casey,** secretary in NIDDK's Mathematical Research Branch, retired June 30, after 20 years of federal service. She joined NIDDK in 1974 as a "floater" working for the Laboratory of Biochemistry and Metabolism and the Laboratory of Chemistry. In 1975, she was offered a full-time position as secretary to the chief of the Mathematical Research Branch, where she remained until her retirement. Her retirement plans include volunteer work, painting and traveling ... **Norma L. Guenterberg,** secretary to Terry F. Pechacek in NCI's Smoking, Tobacco, and Cancer Branch, retired Apr. 30 after 27 years of government service ... **Edna V. Jacobs Hill**, a biochemistry lab technician in NIDDK's Laboratory of Cellular and Developmental Biology, retired on June 3 after 32 years at NIH. She came to NIH in 1958 and worked in the Veterinary Resources Branch, Division of Research Services. In 1960, she joined NIAMD (now NIDDK) and worked there until her retirement. She has many interests that she hopes to pursue and also hopes to do more traveling and camping ... **Dr. Helen Lloyd** has retired after 39½ years at NIH. She came to NHLBI's Laboratory of Chemistry in 1951 in the USPHS as a senior assistant scientist under Evan Horning. She left for a short time and then returned to work in the Laboratory of Chemistry, NHLBI, now the Laboratory of Biophysical Chemistry. In retirement, she plans to move to Sequim, a peninsula in the state of Washington, where she has friends ... **Winnie Lumsden** retired after nearly 29 years of service in the federal government, most recently as NCI's committee management officer. Since December 1980, she has managed the institute's public advisory committees ... **Beatrice (Bea) McKinley,** senior administrative officer in the Management Services Branch of NIAID's Office of the Director, has retired after a 22-year career at NIAID. She will spend much time traveling ... **Helen G. Orem** retired June 1 from her position at the Clinical Center. She established the Clinical Center Art Galleries in 1987. The galleries offer the works of local artists for sale with a portion of the proceeds benefiting the Patient Emergency Fund. In 1984, she began the Clinical Center Art Program, which has flourished into a collection of permanent art. She began her career at NIH with the Medical Arts and Photography Branch, DRS. She left to raise her family and returned to MAPB in 1974, where she worked until joining the Clinical Center in February 1987 ... **Dr. Kendall G. Powers,** a DRG health scientist administrator, retired after 42 years of active and reserve duty in the USPHS ... **Charles Pyles**, known as Charlie, has retired after 31 years in NIH's Security Division. Starting out as a guard, he moved into parking and traffic control, then security evaluation. For the past 3 years he has been working in the crime prevention section in the Division of Security Operations. In retirement, he plans to continue working for a private firm doing security surveys ... **Dr. David P. Rall,** director of the National Institute of Environmental Health Sciences since 1971 and also director of the National Toxicology Program since 1978, retired on Oct. 1. His retirement marks the end of an era during which NIEHS grew from a handful of employees housed in leased space with an annual budget of $24 million, to a world center for toxicological research with 1,000 employees and an annual budget of more than $230 million. Prior to his NIEHS appointment, Rall was associate scientific director for experimental therapeutics at NCI. Under his leadership, scientists at NIEHS laboratories as well as at college and university laboratories supported by institute grants and contracts have made major advances in understanding the toxicity of scores of hazardous substances, including the cellular and molecular mechanisms by which environmental contaminants cause illness. Rall was among those to initiate early studies of the hazards of halogenated aromatic hydrocarbons, a family of chemicals including PBB's, PCB's, dioxin and dibenzofurans. Major advances were made in the study of asbestos, vinyl chloride, diethylstilbestrol (DES), cadmium, mercury and lead, among many other examples. He was also instrumental in initiating and supporting landmark studies in the causes and health effects of air pollution. The National Toxicology Program has expanded its series of published technical reports and its archives are among the largest in the world and an invaluable resource for future toxicological studies. Rall has throughout his career been recognized for his leadership role with many awards and honors. He plans to return to Washington, D.C. While a search committee helps select his successor, Dr. David G. Hoel, director of NIEHS' Division of Biometry and Risk Assessment, will serve as acting NIEHS director ... **Barbara B.**

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Shepherd retired June 30 from her position as secretary to the Associate Director, Cancer Prevention Research Program, Division of Cancer Prevention and Control, NCI. She began her career at NIH in 1975. Her son William is an astronaut who just completed a second mission on the recent Discovery space shuttle flight ... **Calvin Waddell,** a computer clerk in the NIGMS Office of Data Management, retired recently after 40 years of government service, 23 of them at NIGMS. Waddell takes great pride in the home that he purchased in Washington, where he plans to spend his retirement working with senior citizens.

DEATHS

Dr. Sidney Blumenthal, 80, an educator, pediatric cardiologist and a former director of the Heart and Vascular Disease Division of the National, Heart, Lung and Blood Institute at NIH in the mid-1970s, died of leukemia June 19 at the Columbia-Presbyterian Medical Center in Manhattan ... **Dr. Murray Bowen,** 77, a psychiatrist who was a pioneer in the use of family therapy to treat mental illness, died Oct. 9 of lung cancer at his home in Chevy Chase. He was on the staff of NIMH from 1954 to 1959 and during that time he was among the first to treat the family unit instead of the individual. After he left NIH he joined Georgetown University Medical Center where he developed and extended his theories about family therapy ... **Beverly B. Cox,** 65, who worked in the computer field at NIH, died of cancer July 7 at the Reston Hospital. In 1962, she joined the staff at NIH and she retired in 1983 ... **Anna B. Edelin,** 77, a retired NIH grants administrator, died Aug. 27 at Shady Grove Adventist Hospital after a stroke. She worked at NIH from 1965 until retiring in 1980 ... **Stanley I. Hirsch,** 74, former chief of NIMH's social services section, died of cancer June 17 at his home in Silver Spring. He had served 30 years in the PHS Commissioned Corps and held the rank of captain. Following his retirement from NIMH in 1981, he served as a guest worker there until shortly before his death. He had joined NIH in 1955 to become chief social worker in the Clinical Center. In 1956, he was named chief of NIMH's social work department. In 1974, he was made patient recruitment coordinator, NIMH. During his years at NIH he was active in the Hamsters Theatre and worked as a volunteer for CFC and Savings Bonds campaigns ... **William Isaac Lourie Jr.,** 73, a retired health statistician at NCI, died of complications from a brain tumor Sept. 19 at the Hebrew Home of Greater Washington in Rockville. He came to Washington in 1940 to work for the Census Bureau as a statistician. During World War II, he served in the Army in the Pacific and twice received the Bronze Star. In 1946, he joined NCI and retired in 1985 ...**Dr. Stevan Milkovic,** 67, died in Zagreb, Yugoslavia, in December 1989 of cancer. In 1969 he came to NIH as an NIH International Postdoctoral Fellow. He worked with Dr. Robert Bates in the endocrinology section of the Laboratory of Nutrition and Endocrinology, NIAMD. Besides continuing his work in fetal endocrinology, he collaborated with Bates on the effects of transplantable mammotropic tumors in rats. He published extensively while at NIH and became well-recognized internationally as an authority on the endocrine aspects of fetal development in experimental animals ... **Dr. Margaret K. Deringer Barrett Miller,** 74, a retired research biologist at NCI, died of kidney failure Aug. 12 at Suburban Hospital in Bethesda. In 1942, she joined the staff of NCI as a research fellow. She retired in 1980 as biologist in the registry of experimental cancers, but after retirement she had continued to do research at the American Institute for Cancer Research ... **Dr. Lot B. Page,** 67, former chief of the Cardiovascular Aging Program at NIA, died of prostatic cancer Aug. 29 at his home in Lincoln, Mass. He worked at NIH from 1985 until 1989, when he became chief of medicine at the Manchester Veterans Medical Center in Manchester, N.H. ... **Dr. Cephas Taylor Patch,** senior investigator in the Intramural Research Program, NICHD, died of cancer July 16, just a few weeks after he had retired. He came to NIH in 1968 as a staff fellow with NIAID and then he was with NCI from 1971 until 1982, when he joined NICHD ... **Gilbert Dean Press,** 59, former budget officer for NIDR, died June 30 of a heart attack. He had more than 30 years of government service when he retired in May 1988. He began his government career in 1955, when he joined the General Medicine Branch at NCI as a medical biology technician. Six years later he advanced to a position as a chemist in what was then NHI and a reassignment in the mid-1960s sent him to NICHD's Gerontology Branch in Baltimore. In 1973 he was accepted into the Management Intern Program and from there he went to the NIDR budget office, where he was eventually promoted to budget officer ... **George E. Presson,** former executive officer of the Fogarty International Center since its inception in 1968, died July 2 at Fairfax Hospital in Falls Church, Va. Before coming to FIC, he headed the management operations section of the Office of International Research. As executive officer at FIC, he designed and implemented the Fogarty Center's administrative management programs. He also formulated a series of guidelines for international conference procedures. He retired after 39 years of government service ... **Dr. Robert L. Ringler,** 68, a retired NIH official, died of cancer Aug. 16 at his home in Big Rapids, Mich. He began his career with NIH in 1961 as a scientist administrator with the National Heart and Lung Institute. In 1969, he was appointed the institute's deputy director. During his last 5 years with NIH, before retiring in 1983, he was deputy director of NIA ... **Dr. Stanley J. Sarnoff,** 73, founding director of a heart research laboratory at NHI and who later started Survival Technology, a health care company, died of heart ailments May 23 at University Hospital in Salt Lake City, Utah, where he had gone for medical treatment. In 1954, he helped set up The Laboratory for Cardiovascular Physiology and he directed it for 10 years. He conducted research on the heart and the circulatory system and had a research fellowship program. In 1964, he resigned and started Survival Technology to make and market an automatic syringe he designed that allows patients to inject themselves. Different ones were produced for heart patients or patients with various allergies. The company also supplied the Army with syringes containing an antidote for nerve gas. The company's other products included monitoring equipment for heart patients. He held more than 40 patents and in 1980, he founded the Stanley J. Sarnoff Endowment for Cardiovascular Science, Inc., to provide research fellowships for medical students ... **Dr. James Allen Scott,** 92, a retired research grants official at NIAID, died of kidney failure Aug. 18 at his home in Bethesda. He was an authority on helminthology. He joined NIH in 1962 and was chief of parasitology and medical entomology in the extramural programs at NIAID. He was also a member of NIH's graduate research training grants committee. He retired in 1972 ... **Betty Smith Spaugh,** 67, of DRG, died Aug. 14 ... **Dr. DeWitt "Hans" Stetten Jr.** 81, NIH deputy director for science, emeritus, died Aug. 28 of congestive heart failure, **see story on page 1 of *Update*.**

Japanese Embassy Hosts Gala NIHAA Reception

On Friday, Oct. 19, the NIH Alumni Association hosted a very successful reception at the Japanese Embassy. The party, attended by NIHAA members, guests, Japanese officials, embassy personnel, and Japanese scientists at NIH, was held at the lovely and historic old ambassador's residence on the grounds of the embassy.

As part of the reception former NIH director Dr. James B. Wyngaarden was honored. His birthday was celebrated with a gift of photos showing the sculptures that were installed at NIH during his tenure. The guests were welcomed and greeted by Minister Hiroshi Hirabayashi, Embassy of Japan, and Vice Minister Isao Hokugo, Ministry of Health and Welfare Department of Japan.

The reception also honored the Japanese scientists at NIH. Three Japanese firms that helped by contributing to the event were: Fujisawa Pharmaceutical Co., Ltd., Otsuka America Pharmaceutical, Inc., and Japan Express Travel. The setting, the camaraderie and the food all came together to make for a very memorable affair.

Photos: Bill Branson

Welcoming guests at party were (from l) Minister Hiroshi Hirabayashi, Embassy of Japan; Dr. James B. Wyngaarden, former NIH director; Dr. Diane Wallace Taylor, Georgetown University, Department of Biology; and Dr. Gordon Wallace, NIHAA president.

Vice Minister Isao Hokugo, Ministry of Health and Welfare Department, Japan, greets guests at the party.

Dr. Gordon Wallace presents a gift to former NIH director Dr. James B. Wyngaarden at a birthday reception held in his honor. Looking on is Harriet Greenwald, executive director of NIHAA and editor of NIHAA *Update*.

Dr. and Mrs. Vaman S. Waravdekar stand before one of the paintings at the old ambassador's residence, Embassy of Japan.