

NIHAA Update

President's NIH Visit Lifts Spirits of Patients, Staff

By Rich McManus

President Bush's 90-minute visit to the NIH campus three days before Christmas left patients and caregivers with a strong impression of the genuine concern and compassion that he, his family and administration have for people with AIDS and their loved ones.

Joined by his wife Barbara, their son George Jr., and DHHS secretary Dr. Louis Sullivan and his wife, Ginger, the president received briefings on AIDS research from top NIH authorities then spent time with both adult and pediatric AIDS patients, urging them to tell him their problems.

"Two things struck me about the president's visit," said Dr. Anthony Fauci, NIAID director and NIH associate director for AIDS research. "First, it publicly confirms what we've all known—that the president is a strong supporter of NIH, particularly of its intramural program here in Bethesda.

(See Visit p. 2)



Lorraine Lamar watches as her son Austin, an AIDS patient, gives President Bush a kiss during his visit to NIH. The President exchanged gifts and holiday greetings with both adult and pediatric AIDS patients here. (Photo from Wide World Photos)

1989—The Year in Review at NIH

By Dr. William F. Raub

Technological advances of the past 15 years have enabled biomedical scientists to progress at unprecedented speed. This rate should continue to increase as the concepts and methods of structural biology, immunology, and molecular genetics find ever-wider application.

During 1989, NIH intramural scientists and awardees scored major successes. For example, a team from the National Cancer Institute and the National Heart, Lung, and Blood Institute transferred cells containing foreign genes into humans for the first time. This use of a tracer gene is a major step toward gene therapy in humans.

In another elegant blend of immunology and molecular genetics, scientists at the National Institute of Arthritis and Musculoskeletal and Skin Diseases used a rat model to clone the gene for the last subunit of the IgE receptor—which plays a central role in initiating allergic reactions—and determined the receptor's complete structure. They then developed a rat-human chimeric tissue culture system that expressed IgE-binding properties characteristic of receptors on normal human cells. This system can now be used to screen for a new class of drugs to block the binding of IgE to its receptor and thus prevent allergic attacks.

A high point of the year was the identification of the cystic fibrosis gene by grantees of the National Institute of Diabetes and Digestive and Kidney Diseases and NHLBI. Once the precise function of the protein encoded by the CF gene is determined, prospects for developing drugs that can be designed to correct the defect will be enhanced significantly. Eventually it may be possible to develop a way to correct the



Dr. William F. Raub

gene itself and thus prevent or cure the disease.

A technique that has revolutionized molecular genetics is the polymerase chain reaction (PCR), which can be used to isolate and make large amounts of a desired piece of DNA in a few

(See Review p. 18)

IN THIS ISSUE

1989—The year in review at NIH	p. 1
President Bush visits NIH	p. 1
NIH grantees win Nobel Prizes	p. 3
In NIHAA Forum, Robert Martin writes on why the overselling of science presents new dangers	p. 4
In NIHAA Forum, a reply by J. Craig Venter to "Why do the human genome project?"	p. 5
Leroy Hood maps sequence of genome's benefits to biology	p. 6
News from NIHAA members	p. 7
Brief time line of NIH discoveries	p. 8-11
Panel looks at ways to strengthen NIH	p. 11
NIH Notes reports on awards and honors, job changes, retirements and deaths	p. 12-16
Calendar of Events	p. 23
Alumni Publications	p. 25
NIH Retrospectives	p. 26
Future plans of the NIH Alumni Association	p. 27

Visit (continued from p. 1)

Second, it was an excellent example of the president's empathy and compassion for all AIDS patients, whether they're children or adults.

"He sent a strong signal," Fauci continued, "that he fully understands that the virus is the enemy, not the people who have the disease."

Particularly moving was Bush's participation in a support group meeting for adults with AIDS on the 11th floor of the Clinical Center.

"The discussion was very open and frank," Fauci recalls. "The president wanted to hear from all of the patients, not just the few who spoke up at first. It wasn't just a quick photo opportunity where he came in, shook hands then left. He asked appropriate questions and insisted on hearing from everybody. Even when his staff told him it was time to leave, he wanted to stay and listen to their problems.

"The men themselves were greatly moved by the obvious compassion of the president," he added. "The exchange was full of warmth."

Fauci, who has twice demurred from Bush's entreaties to become the next



**The first lady enjoys her meeting with a young patient.
(Photo courtesy of the White House)**



NCI director Dr. Samuel Broder (l) briefs the president and first lady on the latest AIDS research advances. Looking on are Dr. Anthony Fauci (c) and DHHS secretary Dr. Louis Sullivan (r). (Photo courtesy of the White House)

NIH director, spoke with the president about recent research advances against AIDS; also offering updates were NCI director Dr. Samuel Broder and Dr. Philip Pizzo, whose NCI Pediatric Branch cares for youngsters with AIDS.

The president publicly declared that Fauci was one of his modern-day heroes during the campaign that landed him in the White House. Fauci confirmed that Bush continues to tap him for opinions on federal biomedical research.

"On the occasions that we meet he always asks me, 'Do you have enough (budget)?' and I tell him that, relatively speaking, yes, we do get a very generous share. But a greater pool (of funds) is needed for all of biomedical research, not just AIDS. I told him that scientific opportunities outstrip available resources at the moment. It's not that the amount of money is not substantial, but when he asks if we could do more good things for people if we had more money, my answer is, 'Definitely.'"

Bush addressed a packed Masur Auditorium audience after his AIDS briefings.

"Two years ago in this very building, I met a person with AIDS who spoke of his prolonged suffering," said the president. "And I've just come from two more meetings—one with a patients' support group and the other a family support group. And both reminded me of the need for compassion and understanding."

He defined understanding as "educating Americans who don't want to help, don't want to become involved because of a misplaced fear. They're afraid of holding an AIDS patient because they're frightened of getting AIDS. Barbara and I want to say, and we hope we can continue to demonstrate this, they are wrong. They're simply uninformed."

The president said NIH employees embody "all year round" the compassion and understanding that characterize the Christmas season.

"Too often we forget the true message of this time of year—that justice and kindness can indeed foster goodwill toward all. You know that message," he concluded. "You live that message."

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 material.

Editor's Note

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NIH Grantees Win Nobel Prizes

Two cancer researchers won the 1989 Nobel Prize in Medicine. **Drs. J. Michael Bishop**, and **Harold E. Varmus**, of the University of California, San Francisco, shared the prize, worth about \$470,000.

The Nobel Prize recognizes the work Bishop and Varmus did in the 1970s. They showed that a *crc*-like gene is present in normal cells of nearly all animals and changed the way scientists thought about cancer.

Both scientists, who have had long-time support from the National Cancer Institute, have Outstanding Investigator Grants. Bishop, since 1971, has received more than \$14 million from NCI. Varmus has received nearly \$6 million from NIH, including more than \$5 million from NCI. As young investigators, both worked at NIH in the 1960s.

Drs. Thomas R. Cech, of the University of Colorado, and **Sidney Altman**, of Yale University, jointly were awarded the \$469,000 Nobel Prize for Chemistry on Oct. 13. Working independently, Cech and Altman discovered that RNA acts as a true enzyme.

This finding upset the idea that protein lies behind every catalytic activity of a cell. The capacity of RNA to function without DNA or protein has implications for evolution that have been both embraced and challenged by evolutionary biologists. The finding may answer the modern version of the old question—Which came first, the chicken or the egg?—giving RNA first place over DNA or protein.

Cech, a Howard Hughes Medical Institute investigator, is also an American Cancer Society researcher. His support from the National Institutes of Health has totaled about \$2.5 million since 1975. Altman's NIH support has totaled about \$3.2 million since 1972.

Sixty-two Americans have won the Nobel Prize for Medicine or Physiology since 1945; 43, or more than two-thirds of them, had either worked at or been supported by NIH. NIH has employed or supported more than half (52) of the 99 scientists worldwide who have become Nobel laureates for medicine or physiology since World War II.

More than half (18) of the 30 Americans who have won the Nobel Prize for Chemistry also had NIH ties. Since World War II, 75 scientists worldwide have received the chemistry prize; 22 of them had been NIH employees or grantees.

Dr. James B. Snow, Jr. To Head New Institute on Deafness

Dr. James B. Snow, Jr., professor and chairman of the department of otorhinolaryngology and human communication at the University of Pennsylvania School of Medicine, has been chosen to head the newest institute at NIH. The new institute, known as the National Institute on Deafness and Other Communication Disorders (NIDCD), was created by Congress in October 1988. He assumed his position on Mar. 1.

Visitor Center Offers Tours

The NIH Visitor Information Center (VIC) in Bldg. 10 is now offering a guided tour of the NIH campus at 11 a.m. every Monday, Wednesday and Friday. The tour begins at the VIC reception desk in the lower lobby of the Clinical Center.

For further information, call 496-1776.

**NIHAA Forum
Is Hype Hip?**

**Overselling of Science
Presents New Dangers**

By Dr. Robert G. Martin

Something new and insidious has crept into the scientific literature—hype. In the past two years, we have heard about the wonders of cold fusion, mammalian DNA replication origins working as plasmid origins, immunological reactions working after the antibody has been diluted away, transgenic mice made by dipping sperm in DNA and fused proteins made by exotic new mechanisms. While one or two of these wonders may yet be true, it will not be because the initial papers proved it so.

One could easily explain each of these ballyhooed disappointments. Errors of judgment happen, even under the cautious system by which each paper submitted to a scientific journal is referred to a cadre of peer reviewers.

But in each of these cases a scientific journal's editor-in-chief was alerted via this system to be skeptical of the results. In several cases, the editor had been specifically warned by reviewers not to publish the article because the science was faulty.

Still, two of the editors chose not only to publish, but also to hype the articles as potentially major discoveries by running covers, commentaries and reviews to promote the article. And when the articles were then taken up by major newspapers, relying as those papers must on the prestige of the publishing journal, the journal editors took credit for the stir created by the publicity, but subsequently denied responsibility for the fiasco when the articles were proven unreliable.

Of course, the editor of a scientific journal can't take responsibility for each

and every article that appears in his journal. No one would argue that he should. But he can take responsibility for the public relations gimmickry he uses to promote his journal. And it is this gimmickry that is new to science—and dangerous.

Mind you, I am not questioning the right of any scientist to issue press releases or call press conferences to promote his work or the company with which he is affiliated. Rather, I worry that not only the lay public, but scientists as well are accepting public relations gimmickry without question.

In an interesting study (unpublished), Dr. J. Lee Rosner has examined the forms of titles used in the biomedical literature over the past 10 years in journals such as the *Proceedings of the National Academy of Sciences*, *Nature*, *Cell* and *Science*. The results are striking. From articles that 10 years ago bore such titles as "Studies on the possible carcinogenic effects of K" or "Investigations of Q" or "Possible interactions of A with B", we now have—almost without exception—active sentence titles such as "K causes cancer", "A interacts with B", or "Q is the secret of life". The data are no more compelling now than then. Rather, these



Dr. Robert G. Martin

titles are a feature of the huckstering that has become a fundamental feature of science.

I don't believe that science, or the scientific literature, has gotten significantly better or worse over the years. The small amount of true fraud that exists now, existed then. As a percentage of the total literature, it may even have decreased. (Don't forget there are those who believe that Mendel cooked his data, which would mean that 100% of geneticists working in the late 19th century were frauds.)

Faulty reasoning, poor editing and inadequate controls are nothing new either. And while my own view is that reviewers have become more careless, that's a minor change by comparison with what I'm concerned with here.

What is new is the interjection of hyperbole by the editors of some of our more prestigious journals into the orderly, if chaotic, process of scientific evolution. *Cell* now seems to have joined *Nature* in the policy of promoting one or two articles per issue with an instant "minireview" analysis, much like the TV commentaries after a presidential address and often with as much insight. The editor of *Science* has initiated a salute to the "molecule of the year" and suggested in an editorial that the human genome project would cure society of homelessness.

Scientific yellow journalism, or should I say scientific Fleet Street editing, is upon us. The examples I have cited are only the tip of the iceberg. I assume the motivations of these editors are entirely laudable—e.g., to promote the sales of their journals so as to keep them financially sound. Still, the practice is detrimental. I, for one, would be just as eager to read the journals in anticipation of convincing data.

Dr. Martin is chief of the microbial genetics section in the Laboratory of Molecular Biology, NIDDK.

NIHAA Forum**The Genome Project: The Opportunity of the Century for Biology and Medical Sciences***By Dr. J. Craig Venter*

In a recent NIHAA Forum, Robert Martin asks, "Why do the human genome project?" The answer depends in part on one's scientific, intellectual and social background as well as medical history. Those who are affected or have family or friends that suffer from one of the more than 4,000 genetic diseases that afflict mankind should be interested in a project that will dramatically speed the understanding of these diseases. Individuals with heart disease, stroke, cancer, Alzheimer's disease, schizophrenia or other disorders with a more complex genetic predisposition might welcome a scientific project that will potentially increase by 3,000 times the rate at which new basic information is obtained on genetics and disease. Others interested in the history of humankind and the evolution of species on this planet have an interest in a program that will produce a complete genome reference sequence for humans and other species including a bacteria (*E. coli*), a yeast (*Saccharomyces cerevisiae*), an insect (*Drosophila*), a worm (*C. elegans*), and another mammal, the mouse. These complete DNA sequences together with sequences obtained from other species have the capability of providing a molecular history of *Homo sapiens*. Such work will answer the questions concerning the existence of unique human genes responsible for the essential differences between humans and other species. If we can identify such unique human genes then understanding their role in the evolution and development of humans will provide

exciting new insights into the meaning and definition of humanness. If, on the other hand, unique human genes don't exist, then the 97 percent of the human genome that has been referred to as "junk DNA" could be of critical importance in providing assembly instructions for the 3 percent of the genome that contains the ~100,000 coding genes.

Some investigators will be interested in the genome project for the excitement and the challenge that goes with the exploration of the unknown (less than 2 percent of human genes have been mapped and only a fraction of those have been sequenced). Some may feel that the increase in the information provided by elucidating the DNA and protein sequence of the estimated 100,000 human genes will move basic science forward at a dramatic new pace. This list could be substantially expanded, but I would not include the reasons that Dr. Martin has apparently gleaned from the press.

Let me expand on some of these topics as it might help to show that Dr. Martin, despite his claim that he understands the science, has gone astray in his reasoning.

Dr. Martin states that gene mapping and sequencing efforts, were funded prior to the conception of the genome project and will continue to be funded without it, and that genetic diseases such as cystic fibrosis are being solved outside of the genome project. While this statement on its own is true, I feel the overall question is one of scale, cost and speed. Currently, only a few of the 4,000 genetic diseases have been traced to a defective gene and this usually has been at a tremendous cost of effort, dollars and time. At this present rate we would be well into the twenty-second century or beyond before we would be at the point for all diseases that we are currently with cystic fibrosis. If one examines the tremendous effort and considerable funding that have been directed to scores of research teams for

work on genetic disorders such as cystic fibrosis, muscular dystrophy and Huntington's disease, it is clear that it would be impossible to duplicate such resources for investigations into most, let alone all, genetic disorders. Also it is not clear that the genetic techniques that helped elucidate the cause of cystic fibrosis will work on all genetic disorders. For example, the Huntington's disease gene has been localized to chromosome 4 since 1983. Subsequently, extensive research has narrowed the search for this gene to ~10,000,000 bases of DNA. However, a region this size could potentially contain hundreds of genes. In a recent lecture at NIH, Dr. James Gusella of Harvard indicated that due to the complex genetics in the region of chromosome 4 where the Huntington's defect has been localized, geneticists have emptied their "bag of tricks" that has been useful in sublocalizing other disease loci. This most likely means that each gene in this large chromosome region must be located, isolated and *sequenced* in order to help identify the Huntington's disease defect. This is a process that could take years for Huntington's disease, and longer for other diseases, where extensive patient populations have not been genetically characterized or are not available. While it is probably too late for the genome project to help with Huntington's disease, it cannot but help substantially with thousands of other diseases. I am certain that once a reference human sequence exists, it will take a matter of months, not years, to localize a disease gene once it has been mapped to a particular chromosome. Should Dr. Martin or others choose that we not proceed with the human genome project as planned, I invite them to justify and explain the delay to the patients and the families of those who will be affected.

Dr. Martin argues, as does Jeremy Rifkin, that because gene therapy is not
(See *Genome* p. 6)

available the primary use of new genetic information will be to increase the number of abortions. This is absurd! How can one be a basic scientist and believe that unraveling the molecular basis of disease will provide only two alternatives: gene therapy or abortion? The ink is barely 6 months old on the cystic fibrosis gene discovery studies and tremendous new efforts are under way to study the chloride ion channel and to develop new pharmaceuticals to be used as therapeutics. This is in addition to efforts under way on gene therapy. This is in fact one of the ways in which the genome project will drive and enhance fundamental research. Each new gene uncovered, whether linked to a genetic disorder or not, will foster new research and discovery. With 100,000 genes in the human genome alone to be characterized, this will absolutely be the most exciting period in the history of science.

The estimates of the amount of money provided by NIH for gene mapping and sequencing exceeded \$523 million in 1989. This does not include the amounts provided by the National Science Foundation or the Departments of Energy or Defense or the multitude of private foundations including the Howard Hughes Medical Institute, the American Heart Association, the Cystic Fibrosis Foundation, etc. How much public debate is there now on the expenditure of these funds or the rest of the multibillion dollar science budget? At the current rate (non-genome project) of sequencing human genes it will take hundreds of years and more than 200 billion¹ (1990) dollars to acquire the sequence of just the coding regions of the genome. It is possible that a number of important genes will never be found by conventional methods. However, new technological advances in all phases of DNA sequencing now make genome sequencing a viable, if not the

¹The amount ~\$200 million/year spent by NIH on human gene mapping and sequencing divided by ~100 new human gene sequences/year times 100,000 genes.

only logical, approach to institute immediately. The possibility of reducing the cost of genome sequencing from \$200 billion to \$3 billion spent over 15 years cannot be ignored. The haploid human genome (3 billion bases) can be sequenced over the next 12-15 years and the sequence can be produced at a steady rate of over 400 million bases/year. This rate is over 300 times the current rate of sequence production (from all species) since 1977, when rapid DNA sequencing was introduced, and over 3,000 times the current rate of human sequence production. Except for a small percent of the total genome budget that was transferred to the National Center for Human Genome Research at NIH, the genome budget is *new* money to NIH, appropriated to the genome project. To suggest that this money would be available to other biomedical research projects if the genome project was cancelled is unrealistic.

The entire cost of the genome project will more than be covered by the expanded tax base resulting from new technology development, new diagnostics and new therapeutics. Last year alone the major pharmaceutical companies paid combined U.S. taxes of \$2.4 billion. The proposed steady state genome budget is \$200 million/year or only a fraction of the existing tax base. If inroads are made on any major disease affecting the U.S. population, the multibillion dollar annual health care budget will likely decrease. If we do not carry out this project in the U.S. then the tremendous economic/technological/medical benefits will be lost to other countries.

The bottom line is that we cannot afford not to go forward with the genome project.

Dr. Venter is chief of the section of receptor biochemistry and molecular biology, and codirector of the Laboratory of Molecular and Cellular Neurobiology, NINDS. He has proposed to sequence the human X chromosome at NIH.

Hood Maps Sequence of Genome's Benefits to Biology

By Rich McManus

The conviction that life, particularly at the molecular level, is just fantastically amazing suffered no tarnishing at the hands of Leroy Hood, a biologist at the California Institute of Technology who recently gave a packed Masur Auditorium audience a glimpse of the brave new world in biology that is aborning with each advance in the human genome initiative.

Armed with twin slide projectors, seamless diction and boundless curiosity and enthusiasm, Hood toured the next 25 years in basic biology and medicine for a crowd assembled for the first of two lectures Hood presented under the auspices of NIDR's Visiting Scholars Program.

"I predict that in 15 years we will have identified more than 100 genes that cause disease and, for the majority of them, we will know how to circumvent the problems," he forecasted. "Medicine will move from its current reactive mode to a preventive mode."

The revolution in biology that began 25 years ago with test-tube DNA experiments is continuing today, he said, powered by sophisticated new technologies "that have profoundly altered the way we do biology": recombinant DNA, monoclonal antibodies and, Hood's specialty at Cal Tech, microchemical instrumentation.

Sequencing all of the DNA in the 50,000-100,000 human genes "is a tool, not a research project," he explained. Although interesting in its own right because it challenges science to find the most accurate and economical method of accomplishing it, the mapping and sequencing project will be most valuable for the experiments and therapies it generates, Hood suggested.

"The first 10 years of the project will be occupied by the development of new technologies," he said. "Clearly, they aren't powerful enough now to mount a frontal attack on the human genome itself."

What biologists aim to discover, ultimately, is how human development proceeds from a single cell to 1×10^{14} cells, all of which interact, more or less harmoniously, with one another. It is this "chromosomal choreography" that is of such surpassing interest.

Humans can make some 50,000-100,000 proteins, which are three-dimensional molecules folded exquisitely into unique shapes. How do genes, which have a single dimension, express these proteins? What is the function of a protein's shape and how does it change over time? The genome project, Hood assured, will help answer these fundamental questions.

"We'll be able to fashion and sculpt proteins not heretofore seen in nature," he predicted.

Two types of maps will emerge during the project's first decade—a physical map, which involves cutting chromosomes into segments and assembling a sort of "linear jigsaw puzzle." The second map will be genetic, showing which genes carry which traits.

"One day we will be able to superimpose the two to find precisely where the gene encoding schizophrenia is located," said Hood.

The genomes of relatively simple organisms will be studied as part of the initiative. Bacteria, yeast, nematodes and flies will be examined for how genes work and how regulatory and functional networks are arranged. The mouse genome will be studied for conserved regions of DNA and as a model organism for human disease.

Beyond the first step of technology development, which Hood said must be made 100 times more powerful than it is today, and the second step of mapping/

sequencing is the problem of data interpretation, which "will be a challenge for many years.

"We should get one-half to 1 percent of the (human) sequence in the first 5 years," Hood said. Regional DNA sequencing will occupy the next half decade. "After 10 years, a very serious attack can be mounted on the remaining 95 percent of the genome."

Primarily interested in studies of the T-cell receptor loci in mouse and man, Hood and his colleagues at the Center for Analysis of Genes and Proteins are devising ever more sensitive and accurate assays for determining protein sequences. In 1986, his team developed a fluorescent DNA sequencer. Today, they are applying better chemistry and computational power to these problems, employing robots and automated protein analyzers to speed their work.

Perhaps the world's most sophisticated computer chip, composed of 400,000 transistors packed into an area of 1 square cm, has been fashioned in Cal Tech labs as a tool for analyzing DNA homology. Two chips, a BISP (biological information signal processor) and FDF (fast data finder), are helping scientists quickly explore thousands of nucleotide base-pairs for regions of similarity.

Hood also described a new test that can determine single nucleotide mutations in DNA—an oligonucleotide ligase assay—which will be an important diagnostic tool in medicine.

Acknowledging that social issues—prenatal diagnosis of disease allowed by DNA technology, workplace discrimination made possible by DNA fingerprinting, as well as new concerns in such areas as insurance and racism—are also factors in the human genome initiative, Hood dismissed them relatively lightly in this discussion. More troublesome, he suggested, is an "abysmal level of science education at the primary and secondary levels in American schools."

News From NIHAA Members

Dr. Peter M. Banks, NCI, Laboratory of Pathology, 1972-74, was just appointed "Director of Anatomic Pathology, and first Frank M. Townsend Professor of Pathology, at University of Texas Health Science Center, San Antonio."

Dr. Maurice Bender, who was at NIH in various capacities from 1958 to 1971, writes: "I am currently spending a great deal of time in overseas travel. Through Elderhostel and other programs my wife & I have visited and studied in Scandinavia, Israel, Russian Soviet Republic, China, Japan and other countries in Europe and across the Mediterranean. In between times I serve on several public and private agency Boards that deal with the problems of the developmentally disabled, the homeless and the elderly."

Dr. Baruch S. Blumberg, who was in the Geographic Medicine and Genetics Section of NIAMD from 1957 to 1964, is now Master at Balliol College, Oxford University for 7 months of the year. He is also still spending part of his time as Distinguished Scientist at the Fox Chase Cancer Center in Philadelphia.

Dr. Bernard Brookman, who was with the Division of Research Grants from 1957 to 1966, writes: "After leaving NIH in 1966, I worked for the Hooper Foundation, University of California, San Francisco, as Associate Director for ICMRT (an NIH grant), retiring from there in 1971. Since then we have lived as retirees in Santa Cruz and in Watsonville, keeping occupied as volunteers in a variety of service programs."

(See *Members* p. 16)

Brief Time Line of NIH Discoveries

Introduction

The NIH Historical Office is compiling a time line of major research accomplishments, primarily focusing on the intramural program. In this issue, we present information from the Hygienic Laboratory period, 1887-1929. Later issues will cover more recent decades. Information has been drawn from many sources, and an effort has been made to link each item with one or more publications. To make this document as accurate and useful as possible, we would solicit your comments and suggestions, which should be sent to: Dr. Victoria A. Harden, NIH Historical Office, Bldg. 60 Room 152, National Institutes of Health, Bethesda, MD 20892.

Part I: 1887-1929

1887

Laboratory of Hygiene founded. Director Joseph J. Kinyoun made the first laboratory diagnosis of cholera in western hemisphere.



1895

Joseph J. Kinyoun launched production of diphtheria antitoxin at the Hygienic Laboratory, one of the first places it was produced in the United States.



1890s

Joseph J. Kinyoun designed the Kinyoun-Francis Sterilizer, a shipboard disinfectant apparatus used effectively for quarantine procedures.



1901

Hygienic Laboratory first recognized in law through an appropriation statute authorizing \$35,000 for a building and charging it with investigating "infectious and contagious diseases and matters pertaining to the public health."

1902

Biologics Control Act stimulated research into biologics products; another act reorganized the Service and authorized the Hygienic Laboratory research program.

1902

Charles Wardell Stiles identified the hookworm as the cause of anemia in the southern U.S. Although this discovery

was made a few months before he joined the Hygienic Laboratory, his subsequent work on hookworm over the next two decades helped to eliminate it as a problem in the South.

1902-03

Julius O. Cobb and John F. Anderson initiated first Hygienic Laboratory studies on Rocky Mountain spotted



fever. Their works launched forty-five years of research on RMSF.

1905

Reid Hunt demonstrated the presence of thyroid hormone in the blood and introduced the acetonitril test for thyroid.

1905

Milton J. Rosenau established the standard for diphtheria antitoxin.



1906

Walter W. King showed the transmission of Rocky Mountain spotted fever by infected ticks to guinea pigs.

1906

Milton J. Rosenau and John F. Anderson published a pioneering study on anaphylaxis.

1906

Reid Hunt discovered the hypotensive effects of acetylcholine.

1906

Milton J. Rosenau, Leslie L. Lumsen, Joseph H. Kastle and other Hygienic Laboratory workers conducted an epochal investigation on the origin and prevalence of typhoid fever in the District of Columbia which became the catalyst for later, broader epidemiological studies.

1907

Joseph H. Kastle developed a reagent for the recognition and estimation of free hydrochloric acid in gastric contents. The reagent he identified became known as "Kastle's reagent."

1907

Reid Hunt described the toxic effects of methyl and ethyl alcohols.

1907

Joseph H. Kastle and other workers in the Division of Chemistry designed a "hemoglobinometer" to measure hemoglobin in blood. An advance over techniques then in use, it became the standard method for several decades.

1908

Milton J. Rosenau and John F. Anderson established the standard unit for tetanus antitoxin.

1908

Arthur M. Stimson developed a better method for rabies vaccine preparation so it could be sent more safely and thus be more widely distributed.



1908

George W. McCoy first demonstrated that rodents were a reservoir of bubonic plague.

1908-1911

John F. Anderson, Leslie L. Lumsen and Wade H. Frost expanded scope of earlier typhoid studies and results of their investigations into stream pollution, milk standards, and water purity became classic examples of epidemiological methods and training.

1909

John F. Anderson and Joseph Goldberger confirmed Charles Nicolle's finding that the body louse was the vector of epidemic typhus fever. They were the first to transmit typhus by direct inoculation of the organisms into experimental animals.

1909

George W. McCoy published a report on 99 neoplasms found in 100,000 rats examined in the plague control investigation in California. This was the first involvement of the Hygienic Laboratory in cancer research.

1910

William H. Schultz described the contraction of the isolated strip of sensitized guinea pig ileum when suspended in a bath of physiological

solution and challenged by specific corresponding antigen. This reaction became known as the Schultz-Dale phenomenon (the "Dale" from the similar work of English physiologist and pharmacologist Sir Henry H. Dale).

1910

John F. Anderson and Wade H. Frost extended earlier studies on hypersensitivity and used for the first time the word "allergen" in reference to allergic antibodies.

1910

Joseph H. Kastle described the oxidases and other oxygen-catalysts concerned in biological oxidations.

1911

John F. Anderson and Wade H. Frost provided the first laboratory evidence of polio infection in persons with non-paralytic disease. This paper was followed by other studies and field investigation in the Hygienic Laboratory on poliomyelitis.

1911

John F. Anderson and Joseph Goldberger first transmitted measles (rubeola) to monkeys by contact.

1911-1914

George W. McCoy, Charles W. Chapin, William B. Wherry, and B. H. Lamb elucidated a new disease, tularemia.

1912

Legislation shortened the name of the Service to "Public Health Service" and expanded the scope of Hygienic Laboratory investigations to include noninfectious diseases and water pollution.

1913-1919

Earle B. Phelps in the Division of Chemistry conducted a series of studies on water pollution and the biochemistry of sewage and industrial wastes which had far reaching importance for pure water.

(continued on p. 10)

1914

Joseph Goldberger identified pellagra as a nutritional deficiency disease.



1914

Walter L. Treadway conducted the first Hygienic Laboratory survey on mental health, studying the role of public and private agencies in ministering to social needs. He continued over the next fifteen years to do surveys on mental health and other problems.

1915

Edward Francis improved the method for embalming, which was of great importance for intrastate shipping of bodies.

1916-1918

During World War I, work by Hygienic Laboratory investigators changed the way smallpox vaccinations were administered to soldiers. They also found that shaving brushes were a source of anthrax and tetanus infections, and production methods were changed.

1917

Mather H. Neill discovered that scrotal reactions of guinea pigs with "Mexican" typhus (later known as murine typhus) could be used as a differential test with "European," or epidemic, typhus. It was first known as the Neill phenomenon (Later called the Neill-Mooser phe-

nomenon after Neill and Herman Mooser, a Swiss pathologist working in Mexico).

1918

Alice C. Evans described the organism that caused undulant fever. Her work hastened the pasteurization of milk in the United States. She also initiated the collection and study of streptococci and their bacteriophages.

1919

Edward Francis extended the earlier observations on tularemia. His other studies, continued into the 1920s, clarified the nature of the agent, its distribution in animals, the role of ticks and deer flies as vectors and the routes of infection in man. The bacterium was later named *Francisella tularensis* in his honor.



1922

Ida A. Bengtson discovered a new variety of *Clostridium botulinum*. This strain was designated as type "C."

1923

William Mansfield Clark alerted the public to the dangers of tetraethyl lead in gasoline, and further field studies, conducted by James P. Leake, set the standards for the safe level of lead in gasoline.

1923

Atherton Seidell developed a physiological test for the activity of vitamin preparations.



1924

Roscoe R. Spencer and Ralph R. Parker produced a vaccine against Rocky Mountain spotted fever, the first human vaccine prepared from the bodies of arthropod vectors.

1925

Joseph W. Schereschewsky, head of a PHS Special Cancer Investigations Laboratory established in 1922 in Cambridge, Massachusetts (in cooperation with Harvard University Medical School), published a statistical review of cancer death figures in the United States, 1900-1920, which increased interest in cancer research.

1925

Charles Armstrong showed that 25% of commercial bunion pads commonly used to cover smallpox vaccinations were contaminated with tetanus spores. His recommendations that such dressings be abandoned saved lives and stimulated the development of the multiple pressure method of vaccination.

1925

Rolla E. Dyer defined the unit for scarlet fever streptococcus antitoxin.

1925

Carl Voegtlin described much of the pharmacology of arsphenamine and related arsenicals.

1926

Kenneth F. Maxcy identified an "endemic" form of typhus fever in the southeastern United States and suggested that some parasite of the rat might be its vector.

1926

James P. Leake wrote the authoritative study on the multiple pressure method of vaccination for smallpox.

1928

William Mansfield Clark published a summary of his classic work during the decade on oxidation-reduction systems.

1920s

Carl Voegtlin, in charge of cancer research at the Hygienic Laboratory, conducted early studies on the biochemistry of cancerous and normal tissue. He also investigated the effects of nutrients—protein, riboflavin and biotin—on liver tumors in rats. These studies were among the earliest on the relationship between nutritional factors and cancer.

1920s

Lewis R. Thompson worked on problems of industrial health and contributed a series of well-known monographs on the health of workers in the dusty trades.

1920s

Lawrence Kolb conducted early studies on narcotic addiction and its relationship to crime and personality. In association with Albert C. Dumez, he was able to produce morphine and heroin dependence in monkeys.

1920s

Ida A. Bengtson and Charles Armstrong worked on the problems of food poisoning and botulism as a result of improperly canned foods. Their work contributed to better and safer methods of canning.

1930

Hygienic Laboratory renamed "National Institute of Health."

Panel Looks At Ways to Strengthen NIH Directorship

By Carla Garnett

NIH's new director should have more authority and a larger salary, according to consensus of the advisory committee on NIH, which conducted an open meeting at HHS headquarters Jan. 29. Chaired by Dr. James O. Mason, assistant secretary for health, and attended by HHS secretary Dr. Louis Sullivan, the committee's primary task is to evaluate present aspects of the NIH director position and recommend measures that would strengthen it.

NIH, which accounts for more than 50 percent of the Public Health Service budget, has had an acting director since July 1989 following the resignation of Dr. James B. Wyngaarden, who had been director for 7 1/2 years. Initial efforts to hire for the position have proved unsuccessful so far.

The 17-member committee, composed primarily of private sector biomedical researchers and academicians, also includes former NIH director Dr. Donald Fredrickson, now of NHLBI's Molecular Disease Branch; NIH acting director Dr. William Raub as well as two recent prospects for NIH director, Dr. Anthony Fauci, NIAID director, and Dr. P. Roy Vagelos, chairman and chief executive officer of the pharmaceutical firm Merck & Co, Inc.

"I want to extend my personal appreciation to each of you for consenting to be a member of this committee on what I consider a very important task," said Sullivan, who greeted the panel. "When I was named as the president's choice for secretary of Health and Human Services, I indicated that one of my top priorities would be to strengthen biomedical research.

"Clearly, we have grown tremendously over the years in terms of budget and staff. Changes have been made. Certainly, some changes have been helpful. Some may not have served well if NIH is to continue to be the premier institute of biomedical research.

"Clearly, the 1990s are different from the 1950s. We need to have at the helm of NIH a very strong individual to recruit the best researchers, to give leadership to the scientists as well as advice to me, the president and Congress."

The first item on the committee's agenda was review of public responses to a notice placed by Mason in the Dec. 27 *Federal Register*.

The notice asked several major questions: What are the forces that brought NIH to the position it currently enjoys as the leader of the nation's biomedical research enterprise? What major challenges will the NIH be facing in the 1990s and beyond? What type of individual is needed to fill the position of director, NIH? What factors are responsible for diminishing the attractiveness of the position of director, NIH? What changes are needed to strengthen the position of director and prepare the NIH for the challenges of the 1990s and beyond?

Public responses to the notice, which were summarized and made available to meeting attendees, were submitted by individuals or groups from such institutions as the Association of American Medical Colleges, the Federation of American Societies for Experimental Biology, the American Heart Association, the American Society for Microbiology and the American Federation for Clinical Research. Most responses were frank and thoughtful.

"The strong federal investment over the past 50 years in support of scientists pursuing basic, nontargeted research" was cited by one respondent as a force that made NIH the nation's leader in biomedical research.

(See Panel p. 24)

NIH Notes September 1989 - January 1990

HONORS AND AWARDS

Dr. Richard H. Adamson, director of NCI's Division of Cancer Etiology, was honored with a Meritorious Presidential Rank Award for "outstanding leadership and accomplishments in the area of scientific management" ... **Dennis E. Barnard**, a biologist in the Veterinary Resources Branch, DRS, was primary recipient of the 1989 Technician Publication Award of the American Association for Laboratory Animal Science ... **Dr. Katherine L. Bick**, NIH deputy director for extramural research and training, received a Meritorious Presidential Rank Award for her "sustained leadership in developing unified NIH-wide extramural policies and procedures" ... **Dr. Arnold Brossi**, deputy director of NIDDK's Laboratory of Analytical Chemistry, will receive the 1990 Alfred Burger Award from the American Chemical Society (ACS) in May. This award, the highest honor in medicinal chemistry, recognizes his many scientific contributions during his 36-year career ... **Dr. Willy Burgdorfer** of NIAID's Rocky Mountain Laboratories was honored by the Infectious Diseases Society of America with the Bristol Award presented at the society's meeting in Houston. The award is presented annually for outstanding contributions to the field of infectious diseases ... **Dr. Sheldon G. Cohen**, scientific advisor to the Office of the Director, Division of Intramural Research, NIAID, received a Special Recognition Award from the American Academy of Allergy and Immunology for his "many years of service dedicated to the Academy and to the field of allergy and immunology" ... **Jasper L. Cummings**, an accounting technician in the Division of Financial Management, recently received a humanitarian award and medal from the Venerable Order of St. Francis of Assisi for his work helping those in need ... **Dr. Marinos Dalakas** of NINDS's Medical Neurology Branch was presented the "1989 Academy of Achievement Award" by the American Hellenic Educational Progressive Asso-

ciation for his contribution to medical science, especially his original description of and research on post-polio syndrome ... **Dr. John W. Daly**, chief of NIDDK's Laboratory of Bioorganic Chemistry, earned a Meritorious Presidential Rank Award for his role as "an international leader whose career has been devoted to the advancement and extension of knowledge in the field of pharmacology and to the discovery of new, often unique, agents for use in the investigations of physiological and pharmacological function of living organisms" ... **Dr. Igor B. Dawid**, chief of NICHD's Laboratory of Molecular Genetics, received on Oct. 21 an honorary doctorate from the University of Lausanne in recognition of his research on our understanding of gene regulation, especially during embryonic development ... **Dr. Jonas H. Ellenberg**, chief of NINDS's Biometry and Field Studies Branch, received a Meritorious Presidential Rank Award for his "achievement in the publication of outstanding and highly influential contributions in applications of statistics to public health research" ... **Dr. Anthony S. Fauci**, director of NIAID and NIH associate director for AIDS research, received several awards: the William Beaumont Award of the American Medical Association, the 1989 Achievement Award of the American Association of Physicians for Human Rights, the 1989 National Medical Research Award of the National Health Council, and the Maxwell Finland Award of the National Foundation for Infectious Diseases ... **Dr. Joseph F. Fraumeni, Jr.**, associate director of NCI's Division of Cancer Etiology, received the Gorgas Medal at the annual meeting of the Association of Military Surgeons for "distinguished work in preventive medicine that has had a profound effect on the understanding of the epidemiology and etiology of diverse types of cancer" ... **Dr. George J. Galasso**, NIH associate director for extramural affairs, was honored by the Italian government for his accomplishments in the international scientific area and, in particular, to the Italian scientific

community ... **Dr. Harry V. Gelboin**, chief of the Laboratory of Molecular Carcinogenesis, NCI, presented two honorary lectures on a recent trip to Japan, as recognition for individual excellence in cancer research ... **Geoffrey E. Grant**, NIH grants policy officer and acting executive officer for NIDCD, recently received the Hartford-Nicholsen Award from the Society of Research Administrators (SRA) for "his willingness to experiment with innovative ideas (which) has helped to standardize and streamline the administration function, while improving research productivity" ... **Dr. Robert W. Gwadz**, head of the medical entomology unit, malaria section, in NIAID's Laboratory of Parasitic Diseases, was the invited speaker at the Centennial Symposium of the Entomological Society of America. In his talk titled "Insects and Public Health," Gwadz described how insect and arthropod-transmitted diseases affect our lives today and have done so throughout the course of human history ... **Dr. Jin H. Kinoshita**, NEI, was honored for his many contributions to vision research at an international symposium held at Columbia University's Arden House. Papers from the symposium will be published in *Experimental Eye Research* as a *festschrift*, a volume of scientific papers collected as a tribute to a scholar. Among his research accomplishments is defining the role of the enzyme aldose reductase in the development of a diabetic cataract and other complications associated with high blood sugar levels. He left his position as NEI scientific director in June. He is continuing his research at the institute as chief of the Laboratory of Mechanisms of Ocular Diseases ... **Dr. Ruth L. Kirschstein**, NIGMS director, is one of the "100 Most Powerful Women" featured in the September, 1989 issue of *Washingtonian* magazine. She also was selected by the Office of Personnel Management for the 1989 "Profiles in Excellence" series. She was cited for leadership that "established an international reputation for the institute and built consensus and support in the scientific community and Congress" ... **Dr. Michael J. Lenardo**, a senior staff fellow

in NIAID's Laboratory of Immunology, was granted an Investigator Award from the Cancer Research Institute for his "contributions to, and promise in, the field of immunology" ... **Dr. Donald A. B. Lindberg**, director of NLM, received the Nathan Davis Award from the American Medical Association. He was one of the first recipients of the award, which recognizes achievements in furthering "the art and science of medicine and the betterment of public health." He also received the Walter C. Alvarez Memorial Award, which was presented by the American Medical Writers Association in Boston for his "excellence in communicating health care advances and concepts to the public, and for distinguished service to the medical profession" ... **Dr. Lance A. Liotta**, chief of the Laboratory of Pathology, NCI, shared the Dr. Josef Stein Prize for 1989 for leading the research team that discovered and isolated five gene products that play a role in cancer invasion and metastasis. These gene products have proven useful in cancer diagnosis and are the targets of experimental treatments for metastasis ... **Dr. Harald Løe**, director of NIDR for the past 7 years, was appointed Commander of the Royal Norwegian Order of Merit by King Olav V of Norway. At a ceremony in the Embassy of Norway in Washington, D.C., he was presented with a gold cross and a diploma citing his contributions to the field of dental research both in the United States and in Norway. He is an internationally renowned expert on periodontal disease. ... **Dr. Mark L. Mayer**, NICHD scientist, received the Young Investigator Award from the Society for Neuroscience at its annual meeting in October for "his truly important work on NMDA receptors" ... **Dr. John D. Minna**, chief of the NCI-Navy Medical Oncology Branch, NCI, is the recipient of a 1989 clinical research award of \$50,000 from the Milken Family Foundation ... **Dr. Jay Moskowitz**, NIH associate director for science policy and legislation, received the Meritorious Presidential Rank Award for "outstanding leadership and significant accomplishments in the area of scientific policy as

Associate Director for Science Policy and Legislation and as a member of the NIH scientific community" ... **Dr. Abner L. Notkins**, director of intramural research for NIDR and a captain in the PHS, was named winner of the Philip Hench Award by the Association of Military Surgeons of the United States for his outstanding contributions in the field of rheumatology and arthritis by discovery of a component of the immune system and for providing new insight into the nature of rheumatoid factor. ... **Dr. Roger Porter**, deputy director of NINDS, received the Distinguished Medical Alumnus Award for his contributions to medicine from his alma mater, Duke University ... **Dr. David P. Rall**, director of NIEHS and the National Toxicology Program, was honored with the international Ramazzini Award of the Collegium Ramazzini from the town of Carpi, Italy, for his career contributions to occupational and environmental medicine ... **Dr. A. Hari Reddi**, chief of the bone cell biology section, Laboratory of Cellular Development and Oncology, NIDR, delivered the Sarnat Lecture at the Maurice and Gabriela Goldschleger School of Dental Medicine in Tel Aviv, Israel ... **Dr. Marc Reitman**, a postdoctoral researcher in NIDDK's Laboratory of Molecular Biology, received a Lucille P. Markey scholar award in biomedical science to enable him to continue his research on the organization of the beta-globin locus in chickens. He plans to characterize the regions of DNA that are important for the regulation of the beta-globin genes as a group ... **Dr. Steven M. Schnittman**, a senior staff fellow in NIAID's Laboratory of Immunoregulation, was granted one of four prestigious 1989 Young Investigator Awards from the American Society for Microbiology. His research on the immunopathogenesis of human immunodeficiency virus has significantly enhanced the understanding of how HIV causes damage to the immune system ... **Dr. Thomas A. Waldmann**, chief of the Metabolism Branch, NCI has been awarded \$250,000 for basic research from the Milken Family Foundation ... **Dr. Douglas B. Walters**, head of chemical health and safety for the National Toxicology

Program, part of Division of Toxicology Research and Testing at NIEHS, has been named the recipient of the 1989 national award for chemical health and safety from the American Chemical Society ... **Dr. Robert Wurtz**, chief of the NEI Laboratory of Sensorimotor Research, has been elected president of the Society for Neuroscience, a national organization with a membership of 14,000 scientists and physicians. He will begin his term as President in November 1990.

APPOINTMENTS AND PERSONNEL CHANGES

Diane E. Armstrong has been named director of NIH's Division of Equal Opportunity. She has worked for the federal government for 30 years and most recently she served as chief of the Equal Opportunity Division for the Office of Personal Management... **Dr. Carl Banner** has joined the Neuroscience and Neuropsychology of Aging Program at NIA as a health scientist administrator. He was previously a senior staff fellow in the Laboratory of Molecular Biology at NINDS. At NIA, he will direct the extramural research program on the etiology of Alzheimer's disease... **Kenneth Bastin** has been chosen chief of the spiritual ministry department at the Clinical Center... **Dr. Claudia Baquet** has been selected as associate director for the Cancer Control Sciences Program in NCI's Division of Cancer Prevention and Control. Prior to her appointment, she was chief of DCPC's Special Populations Studies Branch... **Dr. Faye J. Calhoun** has been appointed deputy chief for review in DRG's Referral and Review Branch. She came to the division in 1982, serving as executive secretary of the toxicology study section until 1987, when she became acting chief of the physiological sciences review section, RRB... **Dr. Marvin Cassman** has been named deputy director of NIGMS. Prior to this appointment he served as director of NIGMS' Biophysics and Physiological Sciences Program... **Dr. Deborah L. Claman** has joined the NIA as a health scientist administrator for the Neuro-

(continued p. 14)

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science and Neuropsychology of Aging program. She came to NIA from the Office of Scientific Affairs at the National Institute of Alcohol Abuse and Alcoholism, where she was an extramural staff fellow, serving as an executive secretary for the neuroscience and behavioral research review group... **Dr. Lois K. Cohen** has been named extramural program director at NIDR. For the past 6 years she has served as NIDR's assistant director for international health, and chief of the Office of Planning, Evaluation and Communications. She succeeded **Dr. Marie U. Nylen**, who retired in July 1989 ... **Dr. Gyorgy Csako** of the clinical chemistry service at NIH, and who worked at NIH for 10 years, left to accept a staff position at Vanderbilt University's department of clinical chemistry... **Dr. Greg Curt** has been chosen clinical director of the National Cancer Institute. In addition to representing NCI's clinical perspective for the NIH community, he will supervise clinical care and medical training for the institute... **Sheldon A. Fishman** has been appointed chief of the research data and management information systems section in NIDR's Office of Planning, Evaluation and Communications. He succeeds **Dr. Kenneth C. Lynn**, who recently retired... **Dr. Ronald G. Geller** has returned to NHLBI as director of the Division of Extramural Affairs, which is responsible for advising the institute director on research contract, grant, and research training program policies; initial scientific merit review of applications and proposals; managing and processing grants and contracts; and representing the institute on overall NIH committees on extramural programs... **Dr. Robert A. Goldstein** has been appointed director of the Division of Allergy, Immunology and Transplantation for NIAID... **Dr. Albert D. Guckes** has been named deputy clinical director and chief of NIDR's patient care and clinical studies section. Prior to this appointment, he served as chief of NIH's Commissioned Officers Dental Clinic. He replaces **Dr. Michael Roberts**, who retired ... **Dr. Benjamin F. Hankey**, appointed chief of the Cancer Statistics

Branch in NCI's Division of Cancer Prevention and Control, which oversees NCI's Surveillance, Epidemiology, and End Result Program and a variety of other survey and analytical work related to cancer surveillance. He replaced **Dr. John L. Young**, who has joined the cancer surveillance section of the California Department of Health Services, Emeryville, Ca... **Dr. Mark Israel**, head of the molecular genetics section of the Pediatrics Branch of NCI since 1984, has been named director of the new Preuss Laboratory of Brain Tumor Research, which is part of the University of California, San Francisco's Brain Tumor Research Center... **Dr. Leamon Lee** has been selected as the director of NIH's Division of Financial Management. He comes to NIH from Wright Patterson Air Force Base in Dayton, Ohio, where he had been working since 1961... **Dr. Young Jack Lee** has been named chief of the Biometry and Mathematical Statistics Branch in the Prevention Research Program at NICHD... **Dr. Catherine Lewis** was named a program administrator in the Genetics Program, NIGMS. In her new position, she will administer grants in the area of chromosomal organization and mechanics... **Dr. Michael D. Lockshin**, an authority on systemic lupus erythematosus, has been appointed director of the extramural program at NIAMS. Before coming to NIAMS, he was professor of medicine at Cornell University Medical College; attending physician and associate scientist at the Hospital for Special Surgery and a consultant in rheumatology at Memorial Hospital Sloan-Kettering Cancer Center... **Kathryn L. McKeon** has been named associate director for nursing at the Clinical Center. She has served at NIH for 10 years as chief of the mental health, alcohol, neurology, and aging nursing service and most recently as acting director for nursing... **David L. Mineo** has been appointed chief of the Grants Management Branch within the Division of Extramural Research and Training, NIEHS... **Dr. Anthony René** has been named to fill a newly created position, assistant director for referral and liaison, at NIGMS. Prior to this appointment, he

was chief of NIGMS Office of Review Activities... **Dr. Maryann Roper** was named NCI's deputy director on Oct. 8, after serving as acting director since October 1987. She joined NCI in 1985 as a senior investigator in the biologics evaluation section of the Cancer Therapy Evaluation Program. Afterwards, she became special assistant to the director of NCI in October 1986. She will, however, be leaving NCI in the future because her husband, **Dr. William L. Roper**, former head of the Health Care Financing Administration and White House adviser, has been selected as director of the Centers for Disease Control in Atlanta, Ga... **Dr. Helen R. Sunshine** has been appointed chief of the Office of Review Activities, NIGMS. She had most recently been chief of the biophysics section and a program administrator in NIGMS Biophysics and Physiological Sciences Program. Prior to that, she was deputy chief of the Office of Review Activities. She worked as a senior staff fellow in NIDDK before joining NIGMS... **Dr. Flossie Wong-Staal**, will be leaving to take the Florence Seeley Riford Chair for AIDS Research at the University of California at San Diego. This endowed chair is one of the few such professorships devoted exclusively to disease. She plans to establish a collaborative program to develop vaccines against the AIDS virus and will continue her work on the genes that regulate the reproduction and activity of the virus.

RETIREMENTS

Dorothy A. Curtis, the administrative officer supporting two major programs at NIDR, the Extramural Program and the Epidemiology and Oral Disease Prevention Program, has retired. She worked at NIH for 28 years, more than 20 of those years with NIDR in a variety of administrative positions. Her future plans revolve around her interests in community work, family and traveling ... **Dr. Donald R. Fox**, chief of the Research Facilities Branch, NCI, has retired. He began work at NCI in 1972. He will join the firm of Maurice W. Perreault & Associates Inc. in Rockville, Md., as senior vice-

president for biomedical resources program and prearchitectural planning ... **Dr. Arthur R. Hand**, a senior research investigator with NIDR, retired from the PHS on Dec. 1 to become director of the central electron microscope facility at the University of Connecticut Health Center at Farmington. He will also have a faculty appointment in the university's department of pediatric dentistry. He has been with PHS and NIDR for more than 20 years and his current field of research is on salivary gland structure and function ... **Clinton Charles Jameson**, who was with Housekeeping and Division of Space Management, retired in December after more than 29 years at NIH. He is volunteering at St. Mary's Catholic Church, N.W. Washington, and then will travel in the South ... **Dr. David F. Johnson**, who was chief of the Laboratory of Analytical Chemistry, NIDDK, retired after 37 years at NIH. He came to NIH in 1952 and went from lab tech to Ph.D. chemist to section chief to lab chief, where he created an atmosphere conducive to scientific discovery... **Dr. Kenneth C. Lynn**, who was with NIDR for 21 years and in the PHS Commissioned Corps for more than 30 years retired Aug. 31. He served as chief of the research data and management information section, Office of Planning, Evaluation and Communications, NIDR. He also developed two online databases for NIDR: NIDR ONLINE and DENTAL-PROJ, which allows information to be distributed beyond NIDR to the research community at large. He will probably continue his affiliation with NIDR as a consultant ... **William Mathews, Jr.**, chief of the Financial Management Branch, NINDS, retired after 34 years with the institute. He spent his first 10 years at NINDS in the intramural research program. In 1965 he became a budget analyst and for the last 10 years has been the budget officer for NINDS ... **Dr. Michael W. Roberts**, NIDR deputy clinical director, retired Nov. 1 from the PHS after almost 25 years in the Commissioned Corps. He joined NIDR in 1981 as chief of the patient care section in the Clinical Investigations and Patient Care Branch. He has continued to hold that

position along with his present one since 1986. He has accepted a position as the graduate program director of the pediatric dental residency program at the University of North Carolina, Chapel Hill. At his retirement party, former Surgeon General C. Everett Koop presented the Surgeon General's Exemplary Service Medal to him ... **Dr. Robert A. Tolman**, endocrinology research program director at NIDDK, has retired. He came to NIH in 1969 as a grants associate in DRG. He became endocrinology program director at NIDDK after a year in the Myocardial Infarction Branch of NHLBI. He was for many years project officer with the National Hormone and Pituitary Program (NHPP). The NHPP collects and distributes pituitary hormones for research to scientists across the country and is an important resource for studies of hormone structure and function. His retirement plans include pursuing his interest in nature and wildlife and he plans to combine this with his other hobbies such as participation in the Montgomery County Barbershop Chorus, travel and volunteer work ... **Thomas A. Wood, Jr.**, administrative supervisor of the NCI cytopathology section since 1982, retired after 32 years of service at NCI. In 1958, he became a biologist in the cytodiagnosis service, Pathologic Anatomy Branch, which later became the Laboratory of Pathology. He served three 2-year terms on the NCI equal employment opportunity advisory group, including one term as the group's chairman.

DEATHS

Dr. Charles E. (Nick) Carter, who served as the scientific director of the intramural research program of NIEHS from 1979 to 1985, died Oct. 31 at his home in Waterville, Vermont. During his long career in science, he did extensive research in biochemistry, pharmacology, and in areas of nucleic acids and chemotherapy ... **Dr. Gary W. Combs**, 45, chief of the Development and Training Operations Branch of the NIH Training Center, DPM, died of cancer Oct. 11 at Sibley Hospital. He was responsible for

shaping the current NIH employee career development program. He implemented a technique for defining managerial competencies that lead to superior job performance and his work in this area enabled NIH to move from a training curriculum based on general management theory to one anchored in specific, performance-based competencies ... **Dorothy M. Grinspoon**, an administrative assistant with NIH from 1967 to 1980, died of cancer Oct. 14 at the home of her son in Bethesda. She lived in Tamarac, Fla. ... **Robert Lee Harding**, 75, of Frederick, a retired structural planning engineer with NIH, died Dec. 8 at Frederick Memorial Hospital ... **Ann Hartwell**, a former executive secretary of the federal government, died Oct. 20 of pulmonary fibrosis. She worked for the federal government for many years. Her first position was in the National Cancer Institute, where she was secretary to the first director, Dr. Carl Voegtlin. It was there that she met her husband, Dr. Jonathan Hartwell, a chemist who headed NCI's natural products division. She went on to join the Office of Interamerican Affairs and later worked in other jobs in the federal government. After she retired, she held various part-time secretarial positions ... **Edith Darby Crusoe Hogan**, secretary to the acting director of the Division of Engineering Services, died Oct. 26 following a brief illness. She transferred to NIH in March 1986, from Walter Reed Army Medical Center and began working in the Design and Construction Branch, Team 1, until her transfer to the Office of the Director, DES, in December 1988 ... **Rose R. Kushner**, 60, died of breast cancer Jan. 7, 1990, at Georgetown University Hospital. She was a writer who became an advocate for a 2-step surgical procedure for breast cancer after her own experience as a patient. From 1980 to 1986 she was a member of the National Cancer Advisory Board ... **Pope Arthur Lawrence, Sr.**, 76, an official of the U.S. Public Health Service who was assigned to the Environmental Protection Agency at the time he retired in 1977, died of lung ailments Sept. 26 at Suburban Hospital in Bethesda. He began

(continued p. 16)

(continued from p. 15)

his career with the PHS in Texas in 1942. He later worked in New Mexico and Utah, and was transferred to Washington in 1952 where he was assigned at different times to NCI and the Office of the Surgeon General ... **Loraine Frances Mahin**, 79, a retired administrative aide with NIH, died of aspiration pneumonia Dec. 10 at Potomac Manor Care Nursing Home in Potomac. Until she suffered a stroke in June, she was writing and illustrating her autobiography ... **Harriet Sayles Page**, 59, a former NCI medical science writer, died of cancer Sept. 4 at Mercy Catholic Medical Center in Philadelphia. From 1980 until 1985 she was the senior medical writer for NCI—analyzing its program, researching and developing speeches and other documents for the NCI director. She left NCI in 1985 to continue a career of freelance writing and painting ... **Dr. Bernard Sass**, 54, a veterinary pathologist with NCI, died of cancer Oct. 13 at his home in Frederick. He has worked at NCI since 1977 as a veterinary pathologist and most recently was on special assignment at the institute's facility in Frederick ... **Dr. Nathan A. Shock**, 83, a pioneer in modern research on aging, died of cancer Nov. 12 at Francis Scott Key Medical Center. In 1941 he joined NIH's first research program on aging. He directed the Gerontology Research Center in Baltimore and in 1975 was named scientific director of NIA. In 1976 he retired, but he remained active in research as scientist emeritus at NIA's Gerontology Research Center, which was renamed in his honor last June ... **Willie White Smith**, 82, a retired research physiologist who had a 34-year career at NIH and NCI, died of pneumonia Aug. 29 at Holy Cross Hospital in Silver Spring. At NIH she had studied the effects of radiation and the role of infection in radiation deaths ... **Ruth Ferguson Wilson**, 79, a political activist, died Nov. 29 at Suburban Hospital in Bethesda. She was the widow of Luke Wilson, who died in 1985 and whose parents, Luke and Helen, donated to the United States government the land on which most of NIH is built.

Members (continued from p. 7)

Dr. Roger A. Brumback, a clinical associate in the Medical Neurology Branch (NINCDS) 1975-1977, writes: "I was promoted to Professor of Pathology at the University of Oklahoma College of Medicine in July 1989. I am also Chief of the Neuropathology Service. I have recently co-edited a book entitled *The Cerebrospinal Fluid* published by Kluwer Academic Publishers. My wife Mary and I have just had published by Year Book Medical Publishers a book entitled *The Dietary Fiber Weight Control Handbook...*"

Dr. Jelleff C. Carr, NIMH, Psychopharmacology Service Center, 1957-63, writes that he is now "Secretary of the International Society of Regulatory Toxicology and Pharmacology."

Dr. Stanley N. Cohen, who was a clinical associate at NIAMD from 1962 to 1964, recently was the recipient of the National Medal of Technology presented to him by President Bush for his work with Dr. Herbert W. Boyer, who also shared the award. They were honored "for their fundamental invention of gene-splicing techniques, which allowed replication in quantity of biomedically important new products, and beneficially transformed plant materials." Drs. Cohen and Boyer also shared the National Biotechnology Award for their work.

Dr. Susan E. Cullen, NCI, DCBD, Immunology Branch, 1974-76, writes: "For the last few years I have had the wonderful opportunity of returning to my NIH home as a member of the Board of Scientific Counselors for DCBD. It has been a great opportunity because I have had a chance to appreciate the intramural effort from a very different point of view than I did when I was there."

Dr. Martin M. Cummings, who was director of NLM, writes: "After 30 years we are moving from Rockville to live in Chesapeake Beach, Md., in the summer and Longboat Key, Florida, in the winter. We hope to keep in touch with NIH through the Alumni Association."

Dr. Norman H. Edelman, a research associate from 1963 to 1965, at the Gerontology Branch of the National Heart Institute was recently appointed dean of UMDNJ-Robert Wood Johnson Medical School.

Dr. Robert H. Friedman, NIDR, research associate, 1970-72, states that he is "Associate Professor of Medicine and Public Health at Boston University School of Medicine and Chief, Medical Information Systems Unit, an R&D laboratory for computer applications in clinical medicine and clinical research."

Dr. Garry A. Gallis, NIAID, staff associate, 1968-70, is Administrative Director of the Duke AIDS Clinical Treatment Unit (NIH-ACTG), the Director of Clinical Research at Duke CFAR, and the Director of Antimicrobial Evaluation Unit.

Dr. William A. Gibson, NIDR, independent investigator, 1964-76, was recently appointed as Assistant Dean, Graduate Studies and Research at Baylor College of Dentistry, in Dallas.

Dr. I. David Goldman, NCI, Laboratory of Chemical Pharmacology, 1966-69, writes: "July 1, 1988, I was appointed Director of the Medical College of Virginia Massey Cancer Center."

Dr. Javier Gonzalez, who was an HSA intern in 1988, writes that he is currently the "Director of the Research Program in Health Sciences, of the

Department of Health and Social Services of the Generalitat de Catalunya in Barcelona.”

Dr. Daniel M. Goodenberger, NCI, Metabolism Branch, 1976-78, writes that his current position is “Assistant Professor of Medicine, Washington University, Assistant Physician and Associate House Staff Director, Barnes Hospital, and Program Director, Pulmonary Fellowship, Washington University School of Medicine.”

Dr. Ronald B. Herberman, NCI, 1966-85, established “the Pittsburgh Cancer Institute (PCI), now an NCI-designated clinical research cancer institute specializing in innovative approaches to cancer research and treatment. Along with directing PCI, Dr. Herberman holds a joint professorship in medicine and pathology at the University of Pittsburgh School of Medicine and serves as a staff physician at Presbyterian-University Hospital of Pittsburgh.” Currently he “serves as principal investigator for a five-year, six million dollar NIH Program Project to elucidate the factors that predispose organ transplant recipients to develop cancer.”

Dr. Bernard L. Horecker, NIAMD, former chief of the Laboratory of Biochemistry and Metabolism, writes: “I will be retiring from my present position as Dean of the Graduate School of Medical Sciences, Cornell University Medical College on October 31, 1989. I will assume the title of Professor Emeritus of Biochemistry on November 1, 1989.”

Dr. Rachel I. Huot, NCI, 1977-82, states that she “Would love to see a job placement section!” (in *Update*)

Dr. Newton E. Hyslop, Jr. an NIAID research associate in the Laboratory of Immunology from 1963 to 1965, reports that since 1984 he has been the chief of

the Infectious Diseases Section at Tulane School of Medicine and since 1987 the principal investigator at the Tulane-LSU AIDS Trials Unit.

Clifford F. Johnson, who was at NIH from 1957 to 1974, writes that he “and Ruth Johnson have recently moved to Oxford, Pa. Thanks to progress in medicine attributable to NIH programs, they continue to cope successfully with the combined chronic assaults of Parkinson’s, rheumatoid arthritis, Paget’s disease, hypertension and bladder cancer. They winter in Naples, Florida.”

Dr. Roger P. Maickel who was section head at the Laboratory of Chemical Pharmacology at the National Heart Institute before he left NIH in 1965, writes: “I am presently wearing two hats. In addition to my academic post as Professor of Pharmacology and Toxicology in the School of Pharmacy and Pharmacological Sciences at Purdue, I also serve half-time as Director of the University Laboratory Animal Program under the Vice-President for Research.”

Dr. Stanley R. Mohler, who worked in the Center for Aging Research from 1957 to 1961, writes: “I worked in the Center for Aging Research when it was new and had only five employees ... Our tasks included promoting and assisting the development of interdisciplinary centers of research on aging (examples - Duke University, Einstein Medical School, and Western Reserve - in 1960 this latter program received a commitment of more than \$2 million, the largest NIH research grant up to that time - so large that Secretary Arthur Flemming, DHEW, personally presented it in a ceremony) ... My NIH experience was a major career opportunity for development. The FAA invited me (1961) to be the Director of its Civil Aeromedical Institute in Oklahoma City and I served there 5 years and transferred to its Washington, D.C., headquarters for

13 more. I am now a professor of Community and Aerospace Medicine, Wright State University.”

Dr. Ernest J. Moore, who was executive secretary and program administrator at NINDS, 1977-83, writes that he “recently completed six years as Chairperson, Dept. of Audiology & Speech Sciences, Michigan State University, East Lansing. He resigned his position as Chairperson (July, 1989), in order to devote full-time to research & teaching. Presently, Dr. Moore is using neurotoxins (e.g., tetrodotoxin) & competitive antagonists for NMDA & Non-NMDA activity at the cochlear hair cell-auditory synapse.”

Dr. W. Glen Moss, who was at NHLBI from 1961 to 1980, writes: “Still working on genealogical background for me and Harriet in family names (Moss, Crow, Roberts, Bastin, Davenport, McCormick, Ringo, Bourn), (King, Landes, Hampton, Worchester, Davis, Vernon). I am 10th generation on this continent in the Moss, Ringo, and Bastin lines.”

Dr. Henry A. Nasrallah, who was a clinical associate in the Division of Intramural Research at NIMH from 1975 to 1977, is currently professor and chairman of the Department of Psychiatry at Ohio State University and is the Editor-in-Chief of *Schizophrenia Research*, now in its second volume.

Dr. John I. Nurnberger, Jr., who was chief of the NIMH Outpatient Clinics, writes that his current title is Professor of Psychiatry and Medical Neurology and Director of the Institute of Psychiatric Research at Indiana University School of Medicine.

Dr. Margaret Pittman, Division of Biologics Standards, 1936-1971, writes that on June 9, 1988, she received “the
(See *Members p. 22*)

Review (continued from p. 1)

hours rather than days or weeks. PCR was invented by scientists at Cetus Corporation, building directly upon results of basic biomedical research that NIH funded over the past several decades. By enabling scientists to detect short pieces of DNA easily with high specificity and sensitivity, PCR can be used in many areas of laboratory and clinical research. These include detecting HIV infection in the critical latent period before antibodies develop; improving the ability to diagnose genetic diseases; determining how frequently oncogene activation contributes to the development of cancer; studying gene expression during early embryogenesis; clarifying evolutionary biology through the study of "ancient" DNA; and identifying—or exonerating—suspects in rape or murder cases.

PCR has had a profound effect on gene mapping and therefore on the joint effort by NIH and the Department of



Dr. Henry Metzger, NIAMS scientific director, and his colleagues determined the complete structure of the IgE receptor that is critical in initiating allergic reactions. They then developed a tissue culture system that expressed human IgE-binding receptors. The system can be used to search for a new class of drugs that will prevent allergy attacks rather than relieve symptoms once an attack has occurred.

Energy to map and sequence the genomes of humans and other important organisms. Last fall, PCR was made the cornerstone of a proposal to "translate" the information from the various physical mapping methods into a common language known as sequence-tagged sites (STS). These sites are short tracts of unique DNA sequence that can be identified by PCR and that can act as landmarks on the physical map. Any piece of DNA that has been tagged with a PCR site can be easily isolated in any laboratory that needs it. Over the next year, we will pay close attention to how well the STS concept is accepted and how it affects strategies for completing the genome project.

The NIH genome program is being led by the National Center for Human Genome Research, which was established on Oct. 1 with Nobel laureate Dr. James Watson as director and Dr. Elke Jordan as deputy director. The center coordinates NIH intramural and extramural genome research, as well as being the HHS focus for federal interagency coordination and collaboration with industry, academia, and non-profit organizations, and with international groups that support genome research. NCHGR also is expanding into areas such as center and training grants; and, starting this fiscal year, at least 3 percent of NIH's genome program budget will be available for projects that address related ethical, legal and social issues.

Personnel Changes

Dr. James B. Wyngaarden, who served as NIH director for more than seven years, resigned effective July 31. He played a key role in shaping the emergence of biotechnology on the national and international scene, led the massive research effort against AIDS from the beginning, and took significant steps to minimize the management of research by others than the scientists.

During his tenure, NIH's overall appropriation doubled, and the intramural budget did almost the same. One of his major accomplishments was initiating NIH's human genome program. He was a very active, influential spokesman for biomedical research and initiated the physician- and dentist-scientist training programs.

Wyngaarden recently was confirmed by the Senate as associate director for life sciences in the Office of Science and Technology Policy at the White House. The nation thus will continue to benefit from his wisdom and dedication.

NIH is fortunate that almost all of the institutes and divisions have regularly appointed directors. This past year, Dr. Samuel Broder, an intramural scientist for 17 years, was appointed director of NCI. He had been associate director for its clinical oncology program; he and his coworkers were the first to find that azidothymidine (AZT) was active against HIV infection and subsequently developed the second anti-AIDS drug, dideoxyinosine (DDI).

AIDS Research

NIH continues to lead the federal government's research efforts against AIDS through studies conducted by our intramural scientists, grantees and contractors. Almost every component of NIH is now involved in AIDS research.

This past year, encouraging progress was made on the drug front. Two multicenter clinical trials—sponsored by the National Institute of Allergy and Infectious Diseases—have shown that AZT can delay disease progression in HIV-infected persons with fewer than 500 T4 cells, whether symptomatic or asymptomatic, with minimal side effects.

One trial showed that AZT significantly slows the progression of HIV disease when given to persons with early AIDS-related complex (ARC). The other study—the largest AIDS clinical trial yet conducted—showed that early treatment

with AZT can slow progression of the disease in asymptomatic HIV-positive individuals with a low T4 count.

These studies support previous recommendations that individuals at high risk of HIV infection should be tested and that those with positive results should be under the care of a physician who can monitor their immune status and recommend appropriate treatment.

As a result of these studies, an estimated 600,000 HIV-infected Americans with early or no symptoms of the disease could benefit from AZT treatment.

NCI intramural scientists have been the leaders in developing and testing anti-retroviral agents for AIDS.

NIAID has established 18 AIDS treatment research programs based in the communities where people with AIDS live and receive their medical care. The program will enlist many community-based physicians and their patients in studies of AIDS drugs. The program will reach out to all persons with HIV infection, including those in

population groups that have been underrepresented in AIDS studies: blacks, Hispanics, women and IV drug users. By participating in these projects, HIV-infected people will gain increased access to experimental AIDS drugs.

Until now, federally funded clinical trials of experimental AIDS therapies have been conducted by investigators at NIH or at university-based research hospitals. Studies conducted by the new community-based programs will complement the academic ones and must meet similar scientific standards.

Industrial Relations

The remarkable biological and technological revolution we have been experiencing has led to new relationships among government, academic and industrial scientists.

Implementing the Technology Transfer Act of 1986, NIH has shown the way among government laboratories in facilitating the transfer of technology to the private sector for further development and commercialization, thanks

primarily to the foresight and efforts of Dr. Philip Chen, NIH associate director for intramural affairs. Currently, the NIH has about 100 CRADA's—cooperative research and development agreements—with industry and an equivalent number in various stages of negotiation. Under a CRADA, federal laboratories and private sector companies conduct research jointly; the company may acquire an option from NIH at the outset to negotiate for exclusive patent rights. As an incentive, federal scientists can receive up to \$100,000 annually as income from such patented, licensed inventions.

A very important CRADA involves a rabbit model for HIV infection that was developed by NIAID scientists. They infected the animals by injecting them with human HIV-infected T cells. The intramural team has identified the parameters of infection necessary for standardized use of this model in AIDS vaccine and drug development and has filed for a patent covering these procedures.

The HIV-infected rabbits do not become ill although their immune systems are altered. However, when the animals are coinfecting with HIV and HTLV-I, a retrovirus that causes an adult T-cell form of leukemia-lymphoma, they show signs of illness including weight loss, diarrhea, neurologic dysfunction and a rapidly spreading adenocarcinoma. This may be akin to the situation in HIV-infected individuals who then become infected with HTLV-I or other pathogens.

One problem with the rabbit model is that its lymphoid cells do not express determinants that react with antibodies directed against human CD4, the receptor by which HIV enters human cells. In an effort to enhance the model's value in testing drugs and therapeutic strategies that are based on blocking the interaction between HIV and human CD4, the NIAID scientists

(continued p. 20)



Transgenic rabbit developed for HIV infection research by NIAID scientists.

(continued from p. 19)

are collaborating with Transgenic Sciences, Inc., which has the expertise to create transgenic animals. The company has already obtained a full-length clone of the human CD4 gene as stipulated in the CRADA. The NIAID scientists will conduct *in vitro* studies of the "candidate genes" prior to any attempts by the company to insert them into rabbit embryos. Since the NIAID scientists do not have sufficient personnel or containment facilities to create and maintain these transgenic animals, this CRADA is a marvelous example of how government and industry scientists can team up to produce an extremely useful tool for biomedical research.

Another exciting CRADA is under negotiation between the Division of Computer Research and Technology and Star Technologies, Inc., to develop a computer specifically designed for simulating the dynamics of macromolecular interactions. The machine, which has a target price of \$150,000, will be one-hundredth the cost of modern supercomputers, yet—for solving these specific problems—will be as powerful as 20 to 30 Cray processors.



DCRT's Dr. Bernard R. Brooks has designed a dedicated computer for macromolecular modeling that will be one-hundredth the cost of today's supercomputers yet be as powerful as 20 to 30 Cray processors.

The heart of the computer—GEMMSTAR—will be custom-designed silicon chips that, when connected, will embody the computation-intensive part of a computer program (Generate, Emulate, and Manipulate Macromolecules) developed by the DCRT scientists. They have applied for a patent for the machine and the chips, which essentially translate the GEMM software into a piece of hardware that can then be plugged into workstations already used by molecular modelers.

GEMMSTAR will be able to handle simulations of proteins and other macromolecules that contain up to 65,000 atoms—a number beyond the realistic capacity of today's supercomputers. This will tremendously increase scientists' ability to simulate the chemical and physical properties of proteins and nucleic acids and to predict or explain their behavior. Thus, GEMMSTAR should be particularly valuable for interpreting crystallographic or nuclear magnetic resonance data for viral proteins such as those in HIV, and for rationally designing effective drugs and vaccines without the time and expense needed to synthesize and test hundreds of compounds in the laboratory. Chemical and pharmaceutical companies and universities are expected to be the major market for this invention.

NIH is developing guidelines for avoiding conflicts of interest on the part of researchers, consultants, and other participants in research projects at awardee institutions. We want to enable the results of government-supported research to move rapidly to commercialization wherever appropriate while simultaneously ensuring that research goals are not unduly influenced by the possibility of financial gain. This is an extraordinarily complex subject and will require considerable consultation with affected parties to find the balance point.

Scientific Integrity

In recent years, several instances of dishonest practices in biomedical science have received considerable publicity. Misconduct in science is rare, but when it occurs it undermines the public's faith and can jeopardize subsequent research and even proper medical treatment. Clearly, promotion of scientific integrity must be a joint effort on the part of the government and the institutions where research is performed.

Secretary Sullivan has issued regulations that became effective in November concerning misconduct in science—that is, the fabrication, falsification, plagiarism or other practices that seriously deviate from those commonly accepted in research activities. This definition does not include honest error or legitimate differences in interpretations of data.

Awardee institutions will have the primary responsibility for promoting scientific integrity and for investigating, reporting and resolving allegations or suspicions of scientific misconduct. DHHS retains the ultimate responsibility and authority for monitoring such investigations and assuming responsibility if appropriate or necessary. Each institution must file an assurance—and update it annually—that it has policies and procedures in place for dealing with and reporting any possible misconduct in science by their staffs.

To monitor and investigate all misconduct in science cases in the PHS—which includes any on the NIH campus and at awardee institutions—the Office of Scientific Integrity (OSI) was established within the Office of the Director, NIH. OSI will collaborate with the Office of Scientific Integrity Review (OSIR), which was established in the Office of the Assistant Secretary for Health Dr. James Mason.

OSIR will develop PHS policies and procedures for dealing with misconduct

in science, see that the PHS research agencies implement them, review OSI's final reports of investigations, and make recommendations to the assistant secretary regarding sanctions.

Use of Animals in Research

It is tragic that, at a time when biomedical research has so much to offer, animal rights activists want to stifle it by intimidating scientists or trying to get laws passed that make it difficult or impossible to use animals in research. We at the NIH believe that the use of laboratory animals is both a scientific necessity and an ethical imperative and that good animal care is an indispensable part of good science.

In 1989 NIH held a conference on modeling in biomedical research. The panel of experts evaluated model systems—including vertebrates and invertebrates, cell cultures and physical analogs, mathematical models and computer simulations—that have been used in two of the most active areas of research, cardiovascular disease and diabetes. They concluded that, although modeling is extremely valuable, the validity of every proposal about the nature and mitigation of human disease must be verified by testing in an appropriate mammalian model system. Furthermore, they believe it is extremely unlikely that these remarkable tools will substitute, to any significant extent, for experimental vertebrate animals anytime in the foreseeable future. This message must be communicated to the public, which is receiving much misinformation about the use of animals in research.

Last April Dr. Wyngaarden approved the NIH Animal Welfare Initiative: 1989-1990 Goals and Action Plan. The plan involves efforts to ensure adequate resources to upgrade NIH's animal care facilities and to train laboratory personnel to improve the standards of animal care.

NIH awardee institutions also must comply with the PHS animal welfare policy on the care and use of laboratory animals. To foster greater understanding and compliance with that policy, NIH continues to conduct regional workshops for administrators and investigators from awardee institutions.

Also in 1989, Dr. Mason appointed Dr. Fred Goodwin, head of the Alcohol, Drug Abuse and Mental Health Administration, and me to cochair a PHS-wide animal welfare working group. We are developing an action plan whereby all PHS agencies will inform the public about the importance of animals in research and testing and about the humane care and use of animals.

Congress amended the Animal Welfare Act in 1985 with the intent of improving standards for laboratory animals. NIH has played an integral role in harmonizing these regulations with the PHS Animal Welfare Policy through consultations with the Department of Agriculture. Parts I and II of the amendments were rewritten and became regulations on Oct. 31. Part III, which deals primarily with the psychological well-being of nonhuman primates and exercise requirements for dogs, is still under development.

We must not let anti-science feelings among a misguided minority clog the engine of biomedical research at a time when it is moving more rapidly than ever before to conquer disease and disability. As we enter the nineties we must also help to upgrade the quality of science education in our primary and secondary schools and stimulate young people from all racial and ethnic groups to seek careers in science and engineering. The health of our nation and the world depends on it.

This article was prepared with the assistance of Bobbi Bennett, Office of Communications, OD.

HHMI-NIH Collaboration Continues

The Howard Hughes Medical Institute-NIH Research Scholars Program is now in its fifth year; 35 new participants recently arrived on campus. The program, formerly run by Dr. George Cahill and now under the direction of Dr. Don Harter, exposes medical students from around the country to intramural research at the NIH campus.

This year the HHMI Medical Student Research Training Fellowship Program began. It enables medical students to conduct research at institutions in the United States apart from NIH. Forty-seven participants form the inaugural class of this program.

R&W Events Hotline

To help keep NIH'ers informed of all that it does, R&W offers a 24-hour hotline. Dial 496-6598 to hear an updated listing of all the fun things R&W has planned for you!

Novello Confirmed as Surgeon General

On Mar. 1, 1990, Dr. Antonia Novello, deputy director of the National Institute of Child Health and Human Development, was confirmed as surgeon general. She will be the first woman and first Hispanic physician to hold the post of surgeon general. Dr. C. Everett Koop, the surgeon general since 1981, resigned Oct. 1, 1989.

Members (continued from p. 17)

Medical Alumni Association of the University of Chicago Medical Alumni Award for Distinguished Service in recognition of contributions of distinction to medicine and society."

Dr. Denis J. Prager, who was at NIH from 1960 to 1983 is currently Deputy Director, Health Program for the MacArthur Foundation. His responsibility is "for funding programs in mental health research and research on the biology of parasitic diseases."

Dr. Mark L. Rosenblum, NCI, Baltimore Cancer Research Center, 1970-72, is currently at the University of California, San Francisco, where he is "Professor of Neurosurgery and Chairman, Joint Section on Tumors of the AANS & CNS."

Dr. Gunnar Ryge, who was at NIH from 1969 to 1972, is "Professor Emeritus, University of the Pacific, School of Dentistry" and "was the recipient of the Research in Prosthodontics Award for 1989, awarded by the International Association for Dental Research at its 67th General Session June 28-July 1 in Dublin, Ireland."

Dr. John L. Sever, who was chief of the Infectious Disease Branch of NINDS, writes: "Retired from NIH in September 1988 to become Professor and Chairman, Department of Pediatrics, George Washington University Medical School, and Senior Vice-President for Medical and Academic Affairs, Children's Hospital, Washington, D.C."

Dr. Mathilde Solowey, who was at NIH from 1959 to 1979, writes that she has held three positions: "(1) from 1980-81 I was a paid research grants consultant to NYU Medical Center (2) from 1981-84 or 85 I was a paid research grants consultant to Mt. Sinai



Gathering at the Cloister on Dec. 8 for a meeting of NIHAA's Washington chapter are (from l) Dr. Abner Notkins, chairman of NIHAA's organizing committee; Dr. Norman Salzman; guest speaker Dr. Purnell W. Choppin, president of the Howard Hughes Medical Institute, and his wife Joan; and Dr. Mary E. Sears. Choppin reported that HHMI will spend some \$264 million in 1990 to support 200 investigators and 1,600 support staff at 44 sites across the United States. HHMI is the nation's largest nongovernmental supporter of medical research.

Medical School (3) from 1985 to date I have worked as a special consultant on a research project on *cluster studies* at the National Multiple Sclerosis Society - This is a volunteer activity rather than a paid service, so that I can take time off as the need occurs and not feel committed as I would if I were paid. I mention these activities ...to indicate to retirees that there is life after retirement from NIH, provided you look for it."

Dr. David A. Stevens, NCI, Viral Carcinogenesis Branch, 1967-69, writes that he is presently Professor of Medicine (Infectious Diseases) at Stanford University Medical School.

Dr. Louis B. Thomas, who was with NCI from 1948 to 1978, writes: "(1) Since retirement, I have been active in the Ft. Collins Lions Club. In particular I have worked with & supported the various programs of the Rocky Mountain Lions Eye Bank, which is located in Denver and serves a large Rocky Mtn.

region including Colorado, Wyoming and parts of Montana & Nevada. (2) In May 1987 I was awarded an Honorary Ph.D (Doctor of Sc.) by the College of Idaho, Caldwell, Idaho. I graduated from C of I in 1940."

Dr. Gary M. Williams, a staff associate at NCI from 1969 to 1971, writes that he is "now Director of Medical Sciences at the American Health Foundation, Valhalla, N.Y." and "in October chaired a working group at the International Agency for Research on Cancer on evaluation of carcinogenicity of pharmaceuticals."

Dr. Dawn Butler Willis, a chemist at NHI, 1957-58, writes: "In 1968 I obtained a Ph.D. in Microbiology from the University of Tennessee. After 20 years of bench research, I recently accepted the position of Scientific Program Director at the new American Cancer Society National Headquarters in Atlanta, Ga."

CALENDAR

FEBRUARY—MARCH

An exhibit on "To Your Health" — historical public health posters from 1900 to 1990 — is on display in the inner lobby of NLM (Bldg. 38 on the NIH campus).

An exhibit on "The History of Cataract Surgery" is on display in the front lobby of NLM. For more information about both exhibits call (301) 496-5405.

APRIL

Monday, April 23-Tuesday, 24, 1990
"The Medicinal Muses: The Therapeutic Uses of the Arts and Humanities." Sponsored by NLM and University of Maryland. For more information please call Robert Mehnert, Public Information Office, NLM, (301) 495-6308.

Thursday, April 26, 1990, 1:30 p.m.
Lipsett Amphitheater, Bldg. 10
The Third Paul Ehrlich Lecture
Sponsored by FAES. Topic: "RNA and DNA Antagonists As Chemotherapeutic Agents." Speaker: Dr. George H. Hitchings, President, The Burroughs Wellcome Fund, Scientist Emeritus, The Burroughs Wellcome Company and recipient of the Nobel Prize in Medicine and Physiology 1988. Reception following at the Cloister.

MARCH—MAY

NIH Consensus Development Conferences

Monday, March 19 -
Wednesday, March 21, 1990
"Surgery for Epilepsy"(Sponsored by NINDS and OMAR)

Monday, March 26 -
Wednesday, March 28, 1990
"Treatment of Sleep Disorders of Older People"(Sponsored by NIA and OMAR)

Wednesday, April 16 -
Friday, April 18, 1990
"Adjuvant Therapy for Patients with Colon and Rectum Cancers"(Sponsored by NCI and OMAR)

Monday, May 21 -
Wednesday, May 23, 1990
"Intravenous Immunoglobulin: Prevention and Treatment of Disease" (Sponsored by NIAID and OMAR)

All of these conferences are held in Masur Auditorium, Bldg. 10. For more information call (301) 496-1143.

NIHAA EVENTS

MARCH

Tuesday, March 13, 1990

A talk with slides by Dr. Fitzhugh Mullan on his book "Plagues and Politics: The Story of the United States Public Health Service" at the Bethesda Naval Officer's Club, from 11:30 a.m. to 2:00 p.m. - reservations necessary. Tickets \$15 per person.

APRIL

Sunday, April 8, 1990

Baroque Music played on period instruments by the Ensemble La Guerre at Strathmore Hall, 10701 Rockville Pike. Preceded by a light buffet 5:00-6:30 p.m. Grosvenor Park Party Room, 10500 Rockville Pike. Limited number of tickets available at \$17.50.

MAY

A "Mixer" sponsored by NIHAA at the American Federation for Clinical Research meetings, May 4-7, 1990, Washington, D.C., will be held on Sunday, May 6, 1990, 5:30-7:30 p.m., in the Wisconsin Room, Sheraton Washington Hotel.

Upcoming in 1990 at NIH - Anniversaries that will be covered in the *Update* are: NIH Credit Union, 50 years, R&W, 45 years, NIDDK and NINDS, 40 years.

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



Two large tulip poplars fell on the roof of the Children's Inn shortly after noon on Tuesday, Nov. 21, 1989, in the aftermath of a windstorm. No one was hurt and damage to the inn was estimated at \$100,000-\$150,000. The opening of the facility was delayed by several months and the inn is now scheduled to open in June 1990.

Panel (continued from p. 11)

Another wrote, answering the same question, "Flexibility in decisionmaking about research programs that has enabled the NIH to respond to changes and opportunities in science."

One public comment, which drew a rebuttal by Secretary Sullivan, read:

"The decline in financial support for the NIH due to reductions in nondefense discretionary spending imposed by the deficit" is a major challenge facing NIH now and in the future.

"That's not really true," Sullivan corrected. "I understand that it may be the perception by some, but in fact the average in terms of dollars (marked for biomedical research at NIH) has actually increased every year. The cost of research outstripped the rate of increase. The cost of specific grants has increased."

Public ideas of what kind of individual the NIH director should be were varied and might also have described superheroes.

According to one respondent, the NIH director should be "imaginative, innovative and creative (able to inspire both lay persons and scientists)."

Another thought the person who directs NIH should be "passionate about the challenge of working cooperatively to resolve differing viewpoints."

A third reply stated that the director should be "possessing of 'limitless energy,' charisma, enthusiasm, and superb interpersonal skills."

Others felt that the position needed to be filled by "a visionary ... who understands what is ideal and what is practical," or one who is "able to approach political issues with 'civic spirit,'" or one who is "understanding of the 'real' world within which NIH functions and therefore be selected from outside the Agency."

The reading of the last comment was followed by laughter from the panel and good-natured debate about what exactly the term "real world" meant.

The next agenda item, a discussion on salary and other compensations for the NIH director, was led by former NIH director Fredrickson. The panel unanimously supported raising the director's salary.

"This is a critical issue," Fredrickson said. "Clearly, we are competing with academic scales and not with other federal positions."

Sullivan agreed with the panel about raising the NIH director's salary but cautioned that conflicts among other federal agencies that also do research may arise, necessitating across-the-board raises.

"The need for salary adjustment is clearly understood," said the secretary, who had just attended a budget press conference where he had announced a \$348 million increase to \$7.9 billion for NIH in fiscal year 1991. "(However), other agencies such as Energy also have similar problems in compensating their scientists."

"We really don't have to look at increasing salaries all across the board," noted Vagelos. "It's really the top level (positions) that suffer."

Fauci put the problem in perspective: "Over the last 10 years, we have been unable to recruit any scientist from the outside at the branch chief level. That is very serious."

Dr. Linda Wilson, president of Radcliffe College, said, "It calls for a bold move, even if one has to label it experimental."

"I think we all agree that this issue is having a chilling effect on the recruitment efforts for this position," concluded Mason.

Another area that reportedly has seemed less than attractive to prospective NIH directors is the amount of authority that the position carries, particularly in the area of disbursing NIH's budget allotment.

To improve the perception that the director has little influence in money matters, the panel proposes to add to the

duties of the position the power to distribute monies from a discretionary fund. A fund in the amount of \$20 million was suggested.

Dr. Samuel Thier, president of the Institute of Medicine at the National Academy of Sciences, described the intent of the proposal:

"The discretionary fund is a mechanism to be used for risk taking and for funding unusual ideas that might not make it through the peer review process."

Setting a term of office for the NIH director was also discussed. Fredrickson advocated a 6-year term.

"I think it's a job that we want to depoliticize," said Dr. Paul Rogers, senior partner for the law firm Hogan and Hartson in Washington, D.C., and a former congressman who had NIH oversight responsibilities. "It's very smart for us to recommend a 6-year term."

Thier, adding his comments on setting a term, shed light on what might be the core of the struggle to find an NIH director:

"It's a question of primary perception. Will it (the position) be seen mainly as an expert in biomedical research or will it be seen mainly as part of the administration?"

The meeting also solicited additional suggestions for strengthening the director's position from the committee and heard comments from observers. The next advisory committee meeting is scheduled for late February.

If you did not receive the first or second issue of *NIHAA Update* and would like a copy, please notify the editor at 9101 Old Georgetown Rd., Bethesda, MD 20814.

Two Publications of Interest to NIHAA Members

Plagues and Politics: The Story of the United States Public Health Service by Dr. Fitzhugh Mullan, which chronicles the 190-year history of the Public Health Service (Basic Books, 224 pages, 215 illustrations, \$26.95).

The Commissioned Officers Association of the USPHS is offering copies of *Plagues and Politics* at a price of \$18.00, which is a saving of 1/3. Requests should be addressed to COA at 1400 Eye Street, N.W., Suite 725, Washington, D.C. 20005, (202) 289-6400.

Mullan will be speaking on Mar. 13, 1990, at a luncheon sponsored by NIHAA at the Bethesda Naval Officer's Club—copies of the book will also be available at that time.

He received his undergraduate degree in history from Harvard University and his medical degree from the University of Chicago. He is trained as a pediatrician. He has been a member in the Commissioned Corps of the United States Public Health Service since 1972. At NIH from 1982 to 1984, he was the chief medical officer at the Office of Medical Applications of Research, OD. His new position is acting director, The Center for Medical Effectiveness Research, Agency For Health Care Policy and Research, Parklawn Building.

Recollections, a new book written by former NIH associate director Dr. Norman Topping with Gordon Cohn, is now available from the University of Southern California.

Topping, who is perhaps best known for his rickettsial diseases research that included preparing an antiserum against Rocky Mountain spotted fever and leading the NIH effort during World

War II to develop a vaccine against epidemic typhus, served as associate director of NIH from 1948 to 1952. He then moved to the University of Pennsylvania as the vice president for medical affairs. In 1958 he was named president of the University of Southern California. From 1970 to 1980 he served as chancellor of USC, and since then has held the post of chancellor emeritus.

Copies of *Recollections* may be obtained for \$18 each by writing to Topping Recollections, 1420 San Pablo Street, Rm. A302, Los Angeles, CA 90033-1042. The FAES bookstore, Bldg. 10, B-1 level, will also be selling the book.

How Many Labs at NIH?

Overall there are 258 laboratories, branches and departments in the intramural program at NIH, with a total staff of 10,862, of whom 1,331 are permanent scientists and 2,717 occupy ceiling-free positions (ones that don't take up an FTE—full-time equivalent—slot). This is according to the minutes of a recent meeting of the scientific directors.

Have You Moved?

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



Accepting an award on behalf of all NIH employees who contributed to the 1990 Combined Federal Campaign is Jack Mahoney, NIH associate director for administration. Phyllis Fleming, CFC associate director for campaigns, presented the CFC Merit Award in recognition of NIH's generous giving—\$664,000, or 102 percent of its goal of \$652,000.

NIH Retrospectives



WINTER 1950

A new Chemical Pharmacology Section has been established by the National Heart Institute, with Dr. Bernard B. Brodie, Associate Professor of Biochemistry at New York University College of Medicine, selected as chief... Mildred Struve, director of nursing services at the Marine Hospital in Seattle, has been appointed first director of Nursing at the Clinical Center. The construction of the Clinical Center was begun on Jan. 1, 1950... Somewhat recovered from their initial venture, "Life at NIH", the Hamsters are coming out of hibernation to discuss their next production for Fall 1950... Dr. Maurice I. Smith, chief pharmacologist, has retired after 30 years with NIH and the old Hygienic Laboratory. He had a temporary "summer position" with the Hygienic Laboratory in 1918, and two years later he left the University of Nebraska to accept a permanent position with the Laboratory... The National Cancer Institute recently awarded grants of \$863,496 to aid laboratory and clinical cancer studies in non-federal institutions.



WINTER 1960

The first eight-carbon sugar to be found in nature has been discovered by scientists at NIAMD. The rare sugar was isolated by Drs. A. J. Charlson and Nelson K. Richtmyer of NIAMD's Laboratory of Chemistry. It has been

found in both the avocado and the sedum plants... Research survey missions took NIH scientists to opposite ends of the earth in recent weeks. Drs. G. Donald Whedon, assistant director, and Heinz Specht, chief of the Laboratory of Physical Biology, both of NIAMD, visited Anchorage and Fairbanks, Alaska, to study the physiological effects of cold. Drs. Elsworth R. Buskirk, physiologist in the Metabolic Diseases Branch, NIAMD, and Dorland J. Davis, Associate Director in Charge of Research, NIAID, were part of a group that visited Antarctica to examine the problems of carrying on research in extremely cold weather areas... Dr. Harry Eagle, chief of the Laboratory of Cell Biology, NIAID, will be the first NIH scientist to present a National Institute of Health Lecture. His topic is "Biosynthesis in Human Cell Cultures"... NIH Director Dr. James A. Shannon, Institute Directors and other staff began testimony before the House of Representatives Subcommittee of the Committee on Appropriations in support of the NIH budget request of \$400 million for fiscal year 1961.



WINTER 1970

Dr. Mortimer B. Lipsett, NCI, will join NICHD to direct and coordinate intramural research on reproductive biology and conception... NIH was awarded the Oliver Owen Kuhn Cup for 1969 by the Bethesda-Chevy Chase Chamber of Commerce for the design of its new research complex, Buildings 35-36-37... Dr. Robert J. Huebner, chief of NCI's Viral Carcinogenesis Branch, was one of six scientists named by President Nixon to receive a 1969 National Medal of Science... Dr. Maitland Baldwin, 51, Clinical Director

and chief of the Surgical Neurology Branch, NIDS, died suddenly of a stroke Feb. 9, 1970. He was one of the founders of NIH's neurosurgery research program, and he also took an active part in creating the Clinical Center Surgical Wing... Dr. Margaret Pittman, chief, Laboratory of Bacterial Products, Division of Biologics Standards, is one of six women in government service who will receive the 1970 Federal Woman's Award for her work in pertussis vaccine standardization and her studies on pertussis and other diseases including cholera, tetanus and typhoid... The Administration's fiscal 1971 budget request for NIH proposes more than \$1.5 billion—an increase of \$103.5 million or about 7 percent over the fiscal 1970 budget request.



WINTER 1980

Revised guidelines for research involving recombinant DNA molecules were published by NIH Director Dr. Donald S. Fredrickson in the Jan. 29 issue of the *Federal Register*... Dr. Thomas A. Waldmann, chief of the National Cancer Institute Metabolism Branch, will give the G. Burroughs Mider Lecture on control of the immune response... Trappist Monk volunteers assist research on the inoculation of humans with the hepatitis B virus vaccine... The U. S. Supreme Court has ruled that grantee research data are not NIH records and are therefore not subject to the Freedom of Information Act. The ruling's effect is that NIH need not insist that grantees hand over data for release to requestors... The President's fiscal year 1981 budget request for NIH is \$3,581.5 million, a net increase of \$138.9 million over the 1980 budget of \$3,442.6 million.

