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NIHAA Update

Julius Axelrod: Portrait Of a Late Bloomer

By Rich McManus

Forty-one years ago, a man who would later go on to win a Nobel prize arrived at NIH with relatively slim prospects for achieving distinction.

Back then, lacking a Ph.D., he was a longshot candidate for success. Today, he concedes resignedly, a man like him wouldn't have a prayer at NIH.

"There are no opportunities in science for a late bloomer now," says Dr. Julius Axelrod, a guest researcher at NIMH's Laboratory of Cell Biology and winner of the 1970 Nobel Prize in physiology or medicine.

"There are a lot of people who mature slowly, and they just don't have a chance," he observed. "You have to have a fast start today—the best schools, the best grades, the best fellowships—or you won't get into the system. I was a good but not outstanding student. Opportunities came and I just made the right choices."

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Dr. Julius Axelrod has, in 41 years at NIH, seen various institutes rise, pioneered in the chemistry of the nervous system and in drug studies, trained scientists, won the Nobel Prize, and, lately, immersed himself in signal transduction research.

Dr. Bernadine P. Healy, formerly of Ohio's Cleveland Clinic Foundation, has been named NIH's 13th director, a position open since August 1989.

Healy Confirmed As Thirteenth NIH Director

By Carla Garnett

On March 21, the Senate confirmed the nomination of cardiologist Dr. Bernadine P. Healy, 46, as NIH's 13th director. She is the first woman to hold the position of NIH director, a post widely regarded in the nation's scientific community as the president's top biomedical research appointment.

Newspapers reported several months ago that DHHS secretary Dr. Louis W. Sullivan had chosen Healy for the job; President Bush officially announced his intention to nominate her Jan. 9.

"Her nomination is good news indeed, and bodes well for the future of the NIH," said Dr. William Raub, who has served as NIH's acting director since August 1989, when Dr. James Wyngaarden resigned.

Healy, who served as an NHLBI staff fellow here from 1972 to 1974, would re-

*(See **Healy** p. 2)*

First Cancer Patients Get Gene Therapy

By Florence S. Antoine

A team of NIH scientists led by immunotherapist and surgeon Dr. Steven A. Rosenberg of NCI treated the first cancer patients in a human gene therapy trial Jan. 29.

Two patients received transfusions of special cancer-killing cells removed from their own tumors and armed in the laboratory with a gene capable of producing a potent antitumor toxin, tumor necrosis factor (TNF).

"This trial will be the first to apply gene therapy to cancer, which, in its many forms, affects millions of people," Rosenberg said.

The cancer-killing cells removed from the patient's tumor are tumor-infiltrating lymphocytes, or TILs, that have migrated from other parts of the body to the cancer site. These cells invade the tumor and may have the ability to recognize and destroy tissue from this tumor that has spread to distant parts of the body.

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turn to NIH from Ohio's Cleveland Clinic Foundation, where she has served as chairman of the Research Institute since 1985. Recently, she has served on several NIH advisory groups including the 1988 panel that debated the use of fetal tissue in federal biomedical research.

Dr. Harvey Klein, chief of the Clinical Center's transfusion medicine department and former Healy associate, also praised the new director. He was a first-year resident with the Osler Medical Service at Johns Hopkins when Healy interned there 1970 to 1971.

Klein said what he remembers most about Healy was her dedication to her patients. "She was extremely conscientious," he said, recalling that Osler interns were required to complete one of the most difficult internships in the country.

"They were supposed to be immediately available, literally all the time," he said. "She was a great favorite among her patients and frequently came in to care for them on her rare time off."

As NIH director, Healy, a 1970 graduate of Harvard Medical School, joins three former classmates already established at NIH—Dr. Michael Gottesman, chief of NCI's Laboratory of Cell Biology; Dr. Herbert Morse, chief of the Laboratory of Immunopathology at NIAID; and Dr. Eric Ottesen, chief of the clinical parasitology section in NIAID's Laboratory of Clinical Investigation.

Gottesman said: "I am delighted that Dr. Healy will be returning to NIH. NIH has done well by our class and we're looking forward to a reunion."

Before directing the Cleveland Clinic Foundation, Healy served as deputy director of the Office of Science and Technology Policy at the White House 1984-1985. From 1977 to 1984 she directed the coronary care unit at Johns Hopkins. A New York City native, Healy graduated from Vassar in 1965.

Stetten Museum Acquires Van Slyke Apparatus

In April the DeWitt Stetten, Jr. Museum of Medical Research will place an original Van Slyke manometric apparatus in the lobby area of the Claude Pepper Building conference center (Bldg. 31, 6th floor). The exhibit will include a brochure that traces the history of this instrument.

Named after the famed chemist Donald Dexter Van Slyke, this instrument, developed in the 1920's, is one of the first devices that successfully integrated modern chemistry with the practice of medicine. As a clinical and research tool, it was distinctive in its versatility, simplicity, and accuracy as a quantitative instrument.

Until the advent of electronic, automated analyzers, which emerged in the 1960's, the Van Slyke manometric device was found in almost every clinical laboratory. Subsequently, however, most of them were destroyed. The instrument in this exhibit was donated to the Stetten Museum by Dr. Rollin Hotchkiss, formerly of the Rockefeller Institute (now Rockefeller University).

To mark the exhibit's opening, Dr. Hotchkiss will give a seminar on research at the Rockefeller Institute during the period of widest use of the Van Slyke apparatus. For more information about his seminar, call Dennis Rodrigues at the Stetten Museum offices, (301) 496-6610.

NIHAA Update

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

Editor's Note

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NIHAA Forum

Zeal in the Office of Scientific Integrity

By Dr. Bernard D. Davis

Since administrators naturally wish to protect their institutions from embarrassment, it is not surprising that they have often been reluctant to respond to allegations of fraud in research. We are now paying a price, as congressional investigations have led to exposure of a substantial number of cases of fraud—more than most scientists would have expected. The increase might only reflect better detection—though it would not be surprising if the frequency had also risen, since standards of integrity have declined conspicuously in our culture (including the highest levels in our government). Nevertheless, the recognition of even a dozen or two cases of fraud, among the 24,000 grants supported by the NIH, does not seriously undermine confidence that the great majority of scientists have extreme concern for scientific integrity, on which their whole enterprise depends.

While this confidence seems to be generally shared by scientists, some legislators have evidently been convinced of a more serious crisis in science. In response to their criticism the Department of Health and Human Services established two new offices: the Office of Scientific Integrity (OSI) in the NIH, and a supervisory Office of Scientific Integrity Review (OSIR) in the department. The latter office not only sets policy but also makes the final decision on the investigated cases.

Since these new offices may significantly affect the future style of research and the relations between scientists and the NIH, they deserve close scrutiny. I shall discuss three aspects of the problem: the effects of dividing the responsibilities between two offices; their very broad mandates; and the zeal of their present administration.

On the matter of structure: while it was obviously necessary to strengthen the mechanisms at the NIH for dealing with fraud, the existence of two offices, for a function that could well be performed by one, wastes both money and time. Moreover, the more elaborate the offices, and the machinery that they require in research institutions, the greater the expenditure. Indeed, since the initial congressional inquiry into fraud was based on the legislators' obligation to prevent waste of taxpayers' money, it would be interesting to compare the cost of the present extensive machinery and activities with the savings.

In addition, if mechanisms for dealing with fraud have the goal of improving the research enterprise, they will not be effective if they are simply imposed as a policing action; they must have the cooperation of the concerned scientific community. The HHS office, lacking the broad connections of the NIH with that community, seems unlikely to be helpful in achieving this goal.

A final comment on the structure of the offices: subordinating the OSI to the OSIR makes the position of its director less effective and less attractive. Moreover, this decision further diminishes the waning authority of the director of NIH—an unfortunate trend in recent years whose negative impact on the attractiveness of that office, and on the status of the institution, is widely recognized.

More important than the structure of the new offices is the second problem, their broad mandate. The groundwork was laid early in the discussions of fraud, when the NIH insisted, on debatable legal grounds, that the term "fraud" must be replaced by "misconduct." Moreover, this term was defined to include not only falsification, fabrication, and plagiarism, but also "practices that deviate seriously from those generally accepted." The Public Affairs Board of FASEB vigorously opposed the change, on the grounds that the term misconduct, and even more the concept of generally accepted practice, are too open-ended in this context. But we lost. Somehow, the old-fashioned term "dishonesty" never got into the act. As George Orwell has taught us, language is important in politics—and "misconduct" has turned out to be an invitation to an ever-expanding scope of government involvement.

Dr. Bernard D. Davis

The resulting mandate charges the new offices not only with monitoring and conducting investigations of misconduct: they should also "promote high standards of laboratory and clinical investigations in science through a prevention and education program." This phrase is fraught with possibilities for encouraging the government to mix problems of misconduct with problems of quality in the conduct of research. And even though the government may enter this area with the wish to be a beloved teacher in a noble cause, its structure inevitably makes its hand heavy.

This is the heart of the problem. The government already has strong and appropriate leverage over quality through

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Integrity *(continued from p. 3)*

the granting mechanism. In addition, it can legitimately investigate and punish fraud. But it is another matter for the government to become involved in pursuing less weighty (and more widespread) faults of scientists such as carelessness, bad judgment, and improper assignment of credit. The need to discourage such behavior and to reward high standards is important, and it is a constant challenge—without expectation of perfect success—to the scientific community, including teachers, referees, editors, department chairs, deans, appointment committees, and granting committees. Moreover, we must concede that recent public attention has been useful in raising consciousness of our need to do better.

Nevertheless, because these problems are inevitably fuzzy and permeate research it seems extremely doubtful that they can benefit from rigid governmental regulations. In our legal system the police require a warrant before they can enter; and without it their presence is no more appropriate in the laboratory than in the bedroom—even when tax money supports the inhabitants.

My third concern is that the broad mandate of these offices is now being pursued with excessive zeal, rather than with restraint. This was originally only a theoretical possibility, but it is now an actuality. NIH training grants already require institutions to provide formal courses in research ethics; and while it is clearly desirable for preceptors to set examples and to engage in discussions that expose their trainees to the canons of ethical scientific behavior, obligatory courses may simply bore students of science, much like required courses in Marxism in some other countries.

An even larger expansion of government intervention is envisaged by the recently appointed director of OSI, Jules Hallum: at the annual meeting of the American Society of Microbiology last May, he suggested that the definition of misconduct should be broadened to include sloppiness, because cutting corners is just as irresponsible as cheating. Moreover, a subsequent PHS document (8/1/90), describing the policies and procedures of the new offices, provided a further innovation: in addition to their own personnel they will require each PHS agency, and each fund-granting component, to designate a Misconduct Policy Officer. Since the OSI should have no difficulty in receiving information about grantees of any branch of the NIH, one must wonder whether the additional branch officers are needed as conduits for such information or are also expected to initiate searches for misconduct.

I conclude that the new offices have become grotesque in their evident aim of purifying science root and branch, without recognition that the cure could do more harm than the disease. This threat to science would seem to merit thorough reevaluation of the offices. Nevertheless, the scientific community has not reacted vigorously. However, a recent lawsuit by a defendant against the OSI has drawn attention to the problem in a way that should promote further discussion. The judge scathingly criticized the process by which the new offices established major new policies and procedures, without public review (*Science* 251:508, 1991).

This judgment will presumably result in publication of proposed policies in the *Federal Register*, inviting public comment. But this contribution of the law, with its traditional emphasis on procedure, will not solve the problem unless the substantive issues elicit comments from scientists on a large scale—whether in response to that publication or through other connections. The main issue is, of course, the need to balance pursuit of fraud with the preservation of an atmosphere that will continue to encourage creativity and boldness in research.

Though the NIH enjoys a respected and even affectionate relationship with the scientific community, it has not always been courageous in defending principles against political pressures. In an earlier era of red-baiting it refused (unlike some other government agencies) to award grants to such distinguished scientists as Linus Pauling and Elvin Kabat, because they were accused (without trial) of political misconduct. To be sure, that shameful action of the NIH does not provide a strong analogy for the OSI and OSIR, since it was based on phantoms, while these offices are addressing real problems. Nevertheless, their overreaction to political pressure is similar—and it threatens the welfare of science on a much broader scale.

Dr. Davis is professor emeritus of bacterial physiology at Harvard Medical School.

R&W Trip to Hawaii

A special trip arranged by the Recreation & Welfare Association of NIH to Hawaii is available to members of the NIH Alumni Association. The tour leaves Dec. 5 from Dulles Airport. The 9-day trip includes tours of Honolulu, a Polynesian luau, a city punchbowl tour, visits to Pearl Harbor and Maui, and a dinner show.

Enjoy the beauty of Hawaii and relax. Whether your pleasure is shopping, swimming, or relaxing in the sun, you are sure to have a wonderful time. Your professional tour guide will be there to assist you. The total price of this trip including airfare, hotels, 8 meals and insurance waiver is $1,679. For further information, contact Kelly McManus or Randy Schools in the R&W office, (301) 496-6061.

News From and About NIHAA Members

Onie H. (Powers) Adams, who worked at the NCI from 1963 to 1967 as a chemist in the Cancer Chemotherapy National Services Center (CCNSC), writes that just before her retirement she was also "at the National Library of Medicine indexing journals for *Index Medicus* and the MEDLARS program." She is now living in Newtonville, Mass. Her husband died in January 1989.

Calvin Baldwin, former NIH associate director for administration and current NIHAA secretary-treasurer, has been appointed to the Bethany Beach, Del., town council. He and his wife, Betty, have a summer home in Bethany. They celebrated their 40th wedding anniversary in March in Bermuda, where they attended an Elderhostel program at the Bermuda Biological Station. The program was an historic and ecological survey of Bermuda and its oceanic environs. They enthusiastically recommend Elderhostel programs to other NIHAA members.

Dr. Samuel Baron was at NIAID from 1955 to 1975, when he retired from the Commissioned Corp, USPHS, and became professor and chairman of the department of microbiology, University of Texas Medical Branch, Galveston. He is still conducting an active research program on host defenses during viral infection and on antiviral agents including interferon. He reports that within the medical school there are several former NIH'ers including Louese McKerlie, who retired from NIH in 1975, and left the department of microbiology in Galveston in 1985, but is still working in the laboratory there. Dr. Brad Thompson, formerly with NCI's Laboratory of Biochemistry, section of biochemistry and gene expression, has been in the department of biochemistry in Galveston since 1984. Dr. Bellur Prabhakar, who left NIDR's Laboratory of Oral Medicine in August 1990, became an associate professor in the department of microbiology.

Dr. Bahige Baroudy, who was at NCI's Laboratory of Molecular Oncology from 1982 to 1983, then in the Laboratory of Biology of Viruses from 1978 to 1982, and then in the Laboratory of Infectious Diseases from 1983 until 1985, is currently director of molecular virology at the James N. Gamble Institute of Medical Research in Cincinnati. He is continuing his research on hepatitis virus, particularly the hepatitis C virus. He loves Cincinnati, says the air is cleaner than in Bethesda, and notes that the parking is easy and there are now direct flights to Europe. He is still playing the violin and enjoys the Cincinnati Symphony Orchestra. He has been joined at Gamble by two other former NIH scientists: Drs. Girish Kotwal and Nafees Ahmad, both of whom left NIAID in 1990.

Dr. R. H. Belmaker reports that he was "a clinical associate at NIMH, 1972-74. I am now chairman of psychiatry, Ben Gurion University School of Medicine, Beersheva, Israel. My main research interest is manic-depressive illness and the biochemical mechanism of action of lithium treatment."

Three former NIH'ers (from l) Dr. Nafees Ahmad, Dr. Bahige M. Baroudy, and Dr. Girish J. Kotwal are pictured in the P-3 biosafety facility at the James N. Gamble Institute of Medical Research.

Dr. Clarence H. Brown III, who was a clinical associate in the Medicine Branch, NCI, from 1968 to 1970, has been named the medical director for Florida's Orlando Cancer Center. The center opened in January through a program linking the University of Texas M.D. Anderson Cancer Center and the Orlando Regional Medical Center. He is a hematologist and oncologist who has been in private practice in Orlando since 1975. He will coordinate the multi-specialty services of about 30 Orlando area physicians who will staff the freestanding ambulatory cancer center.

Dr. Peter E. Dans, a research associate at NIAID from 1964 to 1967, writes that he is now associate professor of medicine at Johns Hopkins School of Medicine and has directed, since 1983, the required first-year course on ethics and medical care. He is also on Maryland's Board of Physician Quality Assurance, which licenses and disci-

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Maryland's Board of Physician Quality Assurance, which licenses and disciplines physicians and other health care professionals. His wife, Colette, who worked at NIAID from 1960 until 1966, is now teaching French in the Baltimore County Public Schools.

Dr. John L. Decker, who recently retired as director of the Clinical Center, was honored when the John L. Decker M.D. Bioethics Resource Center at the CC was officially dedicated on Jan. 11 in recognition of his support of the Bioethics Program. The Bioethics Resource Center will include a library of 300 non-circulating volumes, an online computer network with the Kennedy Institute of Ethics at Georgetown University, a reprint file, a full and complete line of audiovisuals, and it will be coordinated with the NIH Library for literature search services.

Dr. Tom Folks, who was formerly in the Laboratory of Immunoregulation, NIAID, left in October 1988 to go to the Centers For Disease Control in Atlanta as chief of the Retrovirus Diseases Branch in the Division of Viral and Rickettsial Diseases. The research in his laboratory concerns the epidemiology, immunology and virology of HTLV-I and HIV. He still collaborates with colleagues in NIAID. He reports that one of the biggest changes in moving from NIH to direct his own laboratory has involved the increase in administrative responsibilities that take him away from actual bench work.

Dr. Robert P. Friendland writes: "In May 1990, I left the NIA where I was deputy clinical director and chief of the brain aging and dementia section. My new position in Cleveland is clinical director of the Alzheimer Center of the University Hospitals of Cleveland and associate professor of neurology, radiology, and psychiatry in the school of medicine at Case Western Reserve University. I continue to work in neuroimaging research and pathophysiological studies of Alzheimer's disease and brain aging. My wife, Dr. Elisabeth Koss, who was a neuropsychologist in the brain aging and dementia section at NIA and a research advisor for the World Health Organization's Special Programs and Research on Aging (affiliated with NIA) is now a research neuropsychologist in the Alzheimer Center."

Dr. Christian Gillin left NIMH in 1982 to become a professor of psychiatry at the University of California, San Diego (UCSD). He has continued his research on sleep, sleep disorders and the psychopharmacology of sleep. In 1987, he helped found a new journal of neuropsychopharmacology. While at NIH he was a commissioned officer in the PHS and remained in the Naval Reserve in California. He was called to active duty during the recent conflict and is now serving as a captain at the Naval Hospital in Charleston, S. C. in clinical psychiatry. His wife, Dr. Fran Gillin, left NIAID's Laboratory of Parasitic Diseases in 1982 to take a position as adjunct professor in the department of pathology at UCSD medical school's division of infectious diseases. Her research continues to center around the intestinal mucosal parasites such as giardia.

Dr. Joe R. Held, director of DRS from 1972 to 1984, and now vice president for primate operations at Charles River Laboratories in Arlington, Va., received the James A. McCallam Award for outstanding contributions in international veterinary medicine from the Association of Military Surgeons of the United States. This award, which honors Brigadier General James A. McCallam, a former chief of the U.S. Army Veterinary Corps who served in both world wars, honored Held for his outstanding accomplishments in the field of medicine and health.

Dr. Ronald B. Herberman, at NCI from 1966 to 1985, is director of the Pittsburgh Cancer Institute and professor of medicine and pathology at the University of Pittsburgh. He has been named a member of the Pennsylvania Cancer Control, Prevention, and Research Advisory Board, which is part of the Cancer Control Program of the state's health department. It facilitates statewide cancer control efforts, and helps set policy for the state's cancer appropriations.

Dr. Alfred Ketcham, who in his 1957-1974 tenure at NIH was chief of the NCI's Surgery Branch and clinical director of NCI, has been elected president of

the Society of Surgical Oncology. Since leaving NCI, Ketcham has been chief of surgical oncology at the University of Miami and the Sylvester professor of oncology.

Dr. Marilyn J. Koering, who was at NICHD in the Pregnancy Research Branch from 1978 until 1984, is currently professor in the department of anatomy at George Washington University School of Medicine and Health Sciences. She recently had an exhibit of her photographs, entitled "Once Invisible" at the Marvin Center's Colonnade Gallery, George

Koering's photograph shows a magnified sweat gland pore in the palm of a hand.

Washington University. The stunning photographs were done over the past 17 years using a scanning electron microscope. Koering said the "more I looked at them, the more fascinating they became," and realized that she was seeing art, in addition to science.

Dr. Ronald Levy, a clinical associate at NCI from 1970 to 1972 and currently professor of medicine at Stanford University, shared Switzerland's Dr. Josef Steiner Cancer Foundation prize. The 1989 prize was given "for outstanding contributions to cancer research." The foundation stipulates that the prize money must be used for cancer research.

Dr. Frank L. Meyskens, Jr., who was at NCI from 1974 to 1977, is now director of the University of California at Irvine Clinical Cancer Center and chief of hematology/oncology at the UCI Medical Center. He recently received NCI's Year 2000 Award, which recognizes individuals who have contributed significantly toward the national cancer program.

Dr. Howard A. Minners, who was at NIH from 1966 to 1980 (on detail to WHO from 1977 to 1980) writes, "In 1966 I joined the international research programs of the NIH for 11 years with increasing responsibilities. Subsequently, I served for 3 years beginning in 1977 as head of the World Health Organization's research office in Geneva, Switzerland. I returned in July 1980 to become deputy director of the Public Health Service's Office of International Health. In January 1981 I became science advisor to the Administrator, Agency for International Development."

Dr. Paul D. Parkman, who was on campus from 1963 until his retirement in 1990 as director of the Food and Drug Administration's Center for Biologics Evaluation and Research, delivered the invited remarks at the Syracuse Health Science Center graduation awards ceremony in May 1990. He is a 1957 graduate of the medical school.

Dr. J. Palmer Saunders, who was director of the Division of Research Resources and Centers, NCI, from 1956 to 1974, has been named dean emeritus of the Graduate School of Biomedical Sciences at the University of Texas Medical Branch at Galveston. The appointment was effective upon his retirement from the UTMB faculty in November 1990. He has been a professor of pharmacology and toxicology since 1974 and was graduate school dean from 1974 to 1987. In addition to his administrative and research work he has been active in the community. He is a past president of the Galveston unit of the American Cancer Society, treasurer of the University Area Association, trustee of the William Temple Foundation, and president of the Galveston Symphony Orchestra. He also plays trumpet in the Texas Volunteer Band.

Dr. Paul J. Schmidt, who was chief of the blood bank department (now transfusion medicine department) at the Clinical Center from 1954 to 1974, has been since 1975 head of transfusion medicine at Southwest Florida Blood Bank in Tampa. In a recent article in *Florida Business* (March 1990) he was interviewed about his transfusion medicine academic center, which has been established to train health care professionals about the proper use of blood transfusion

therapy: "This blood bank, and blood banking in general, is unrecognizable compared to 1975. For years, transfusion medicine was a support activity. We gave blood to keep patients alive while someone was doing something much more dramatic to them. But now transfusion medicine is recognized as a therapy in itself."

Dr. Boris Tabakoff, until recently scientific director, NIAAA Intramural Research Program, has taken a position as professor and chairman of the department of pharmacology at the University of Colorado School of Medicine. He writes, "The graduate school program in the department has been funded continuously since 1967 by NIH, making it one of the oldest programs receiving continuous support for graduate training in the country."

Science Research Updates

LASER THERAPY EVALUATED AS FIRST-LINE GLAUCOMA TREATMENT

Preliminary evidence from an NEI clinical trial suggests that argon laser therapy may be a safe and effective alternative to eyedrops as a first treatment for patients with newly diagnosed open-angle glaucoma. However, because open-angle glaucoma is a chronic disease with a variable rate of progression, the patients will continue to be followed up to 3 additional years to further assess the value of both treatments. In open-angle glaucoma, the most common form of the disease, minute changes within the eye gradually interfere with the flow of fluids that nourish the tissues in the front of the eye. If these fluids fail to drain properly, the resulting increased pressure inside the eye can eventually damage the optic nerve.

Most eye specialists begin glaucoma treatment with eyedrops, either to improve fluid drainage or to slow fluid formation. Medications, however, must be used daily, can produce annoying and sometimes serious side effects, and sometimes fail to control intraocular pressure. Alternatives include surgery to create a tiny hole in the coat of the eye or laser treatment to do the same thing or to stretch open holes in the drainage tissue.

The Glaucoma Laser Trial (GLT) was designed to evaluate the relative efficacy of medical and laser treatment. All 271 patients received both types of treatment, one type in each eye. If the initial laser surgery failed to control ocular pressure, eyedrops were administered according to a stepped sequence. After 2 years of followup, laser treatment alone was sufficient to control pressure in 44 percent of the eyes, compared to 30 percent of the eyes treated with the antiglaucoma drug timolol alone. The percentage of laser-treated eyes that could be controlled with laser alone or laser with timolol was 70 percent. When eyes in either treatment group required stronger eyedrops, pressure was controlled in 89 percent of those having prior laser treatment and in 66 percent of those who received only medication.

Glaucoma is the second leading cause of blindness among all Americans and the leading cause of blindness among Black Americans. Approximately 4,600 people become blind from glaucoma each year.

HUMAN NEURONS GROW IN CONTINUOUS CULTURE FOR FIRST TIME

Scientists supported in part by NINDS have established the first cell line from human brain cells to survive in continuous culture. Drs. Gabriele V. Ronnett, Solomon H. Snyder, and colleagues at the Johns Hopkins University School of Medicine obtained cells following surgery on an 18-month-old girl to remove brain tissue as a treatment for intractable seizures. The seizures were a result of unilateral megalencephaly, a disorder in which immature brain cells grow and spread abnormally.

The cells grown in culture were neurons, and they expressed neurotransmitters typical of the cerebral cortex. According to the authors, who reported their achievement this spring, the nature of the disease may have made the affected cells uniquely suited to surviving and growing in culture. The availability of cell lines permits a wide variety of studies of cell function and growth; a human brain cell line furnishes an important tool for neurologic research and possibly an avenue for studies aimed at brain tissue transplantation.

CELLS TRANSPLANTED INTO THYMUS OF RATS TRICK IMMUNE SYSTEM INTO TOLERATING THEM AND ANOTHER GRAFT

Transplantation of foreign pancreatic islets into the thymus may provide an avenue for protecting the donor cells from immune rejection, according to research by NIDDK grantees. Transplantation of insulin-producing islet cells is one approach to long-term correction of insulin-dependent diabetes, but rejection of the transplanted islets has been a stubborn obstacle to success. Drs. Ali Naji, Clyde Barker and associates at the University of Pennsylvania, Philadelphia, recently transplanted islets from donor rats of one strain into thymus glands of a different strain of rat. When the transplant was accompanied by an injection of anti-lymphocyte serum that temporarily reduced T cell concentration in the recipient rats, the transplanted islets survived indefinitely without further immunosuppression, revealing the thymus as a new immunologically privileged site for transplantation, at least in rats. (Previously the only demonstrated immunologically privileged sites were brain and testicle.) Even more striking, a second transplant, to a site outside the thymus, of islets from the same donor strain also survived in these rats without immunosuppression. Until now, the first transplant to an immunologically privileged site was usually rejected when a second transplant from the same donor was made to a non-privileged site in the animal.

The research suggests that transplant surgeons may be able to use the function of the thymus in "conditioning" maturing T cells to tolerate tissue transplanted into the thymus as "self" and not foreign. If this approach works in tests in larger animals, it may prove useful in transplantation of other types of cells, as well as organs.

DIABETES ANTIGEN IS NEUROTRANSMITTER-SYNTHESIZING ENZYME

A protein known to be an antigenic target for the destructive autoimmune process in insulin-dependent diabetes (IDDM) has been found to be a key brain enzyme, according to NIDDK-supported scientists.

IDDM results from autoimmune destruction of the insulin-producing pancreatic islet cells. Among the biochemical hallmarks of IDDM are autoantibodies to pancreas-associated antigens, including the so-called 64K protein. The autoimmune destruction begins well before symptoms appear, so autoantibodies characteristic of the disease can be detected in individuals who are at risk for diabetes but have no symptoms. Autoantibodies to the 64K antigen, for example, have been detected in people at risk for IDDM years before the onset of clinical disease, and, for these reasons, the antibodies are an important marker of impending IDDM.

Drs. Steinunn Baekkeskov of the University of California, San Francisco, and Pietro De Camilli of Yale University and colleagues noted that IDDM is common in people with stiff man syndrome (SMS), a rare but serious neurologic disease. Like IDDM, SMS is an autoimmune disease. Most SMS patients have autoantibodies to glutamic acid decarboxylase (GAD), the enzyme that synthesizes the important neurotransmitter GABA (gamma-aminobutyric acid). Both the pancreatic islet cells and central nervous system neurons express GAD. These researchers found that almost all SMS patients also have islet cell autoantibodies. The scientists used immunologic methods to show that the 64K antigen was in fact GAD.

Positive identification of the 64K antigen should both help in the development of techniques for early identification of people at risk for IDDM and aid in discovering how and why the autoimmune process in IDDM occurs. Interrupting the autoimmune attack on GABA may also provide an avenue for prevention of IDDM. For the diabetes community an added dividend of the 64K antigen's new identity is the already intensive research effort under way on GABA and GAD.

GENES FOR KEY IMMUNE SYSTEM ENZYME IDENTIFIED

NIGMS grantees have isolated two genes responsible for producing recombinase, a putative enzyme that clips and joins DNA segments in developing lymphocytes to yield the enormous variety of antibodies and antigen-binding receptors on T cells (thymus-derived lymphocytes).

Dr. David Baltimore, now of Rockefeller University in New York City, and his colleagues at the Whitehead Institute for Biomedical Research in Cambridge, Massachusetts, discovered the two genes, which they named recombination activating genes, or RAG-1 and RAG-2. The enzyme product of these genes—postulated but not yet isolated—stimulates the efficient recombination of three kinds of DNA segments—V (variable), D (diversity), and J (joining)—that, along with the C (constant) segments, are necessary to produce a functioning antibody or a T-cell receptor protein. The many possible combinations of these segments provide the diversity necessary for the immune system to respond to the incredible number of organisms and other proteins that we encounter during life.

Identification of the recombination activating genes is a very important step toward understanding the fundamental mechanisms of the immune system. This work should also contribute to the understanding of inherited types of immune deficiencies, as well as some lymphomas and leukemias.

PHYSICALLY DEMANDING JOBS HAVE LITTLE EFFECT ON PREGNANCY OUTCOME

Long hours of stressful, physically demanding work by pregnant women do not appear to be a risk factor for miscarriage, ectopic pregnancy, premature birth, low birth weight, or stillbirth, according to a large-scale controlled study by NICHD researchers.

NICHD's Drs. Mark Klebanoff, Patricia Shiono and George Rhoads compared pregnancy outcomes of two groups of women: medical residents and the wives of their male counterparts. Out of 4,412 women medical residents studied and 4,236 residents' wives, 989 residents and 1,239 residents' wives completed their first pregnancy during residency and gave birth to a single live infant. While the female residents reported working about twice the number of hours of the employed wives of male residents, there were no differences in the frequency of adverse outcomes of the pregnancies, except in the group of women residents who reported working more than 100 hours per week, especially during the third trimester. These women had an increased risk of preterm delivery (before 37 weeks gestation).

Previous, smaller studies have associated long hours of physically demanding work with adverse pregnancy outcomes but have failed to account for the fact that many women in physically demanding jobs are also poorly educated and paid. The NICHD study eliminated socioeconomic status as a confounding factor by surveying only women of similar economic and educational status. The study suggests that among healthy women who are well educated and who have access to good prenatal care, hard work in and of itself does not compromise the chances that a woman will bear a healthy child.

*(See **Updates** p. 10)*

Updates (continued from p. 9)

TRANSGENIC MICE CREATED FOR SCREENING DRUGS TO REVERSE MULTIDRUG RESISTANCE OF CANCER CELLS

A new line of genetically engineered mice can drastically reduce the number of mice and the time needed for screening new drugs to overcome cancer resistance to chemotherapy.

NCI scientists Ira Pastan, Michael Gottesman and their coworkers produced a strain of mice in 1989 that carries the human multidrug resistance (MDR) gene. The gene is present in all the animals' cells, but it is expressed only in the bone marrow. Expression of the gene protects the bone marrow from the effects of cancer chemotherapy, permitting normal numbers of white blood cells to be manufactured even when the animals are treated with toxic drugs. The gene confers resistance to a number of drugs used to treat cancer, including doxorubicin, vinblastine, and taxol.

These researchers have now shown that the transgenic mice can be used to test agents that can reverse MDR-caused resistance. The MDR gene produces a transporter protein that pumps toxic drugs out of cells, according to the researchers. An important goal of cancer research is to develop safe and effective reversing agents that overcome multidrug resistance by competing with toxic drugs for the MDR transporter. This allows the toxic drugs to remain within and destroy the cells.

Current methods of testing new reversing agents require large numbers of animals (typically 100) and many weeks. Testing with the new mice requires only three to five animals and several days, making it possible to rapidly and less expensively test large numbers of candidate drugs.

TISSUE COMPATIBILITY ANTIGEN MAY CAUSE FORM OF ARTHRITIS

The HLA-B27 tissue antigen, a protein long known to be a genetic marker for a group of arthritic diseases called spondyloarthropathies, may be a major cause of these disorders according to the creators of a newly developed transgenic animal model.

Every person's cells bear a characteristic set of HLA antigens or markers, which play a crucial role in the genetic control and function of the immune system. In work supported by NIAMS and NCRR, researchers used transgenic technology to produce two strains of inbred rats that carry the human genes for the HLA-B27 tissue antigen. To develop their animal model, the researchers inserted two human genes that code for the HLA marker into fertilized rat eggs. Some of the fertilized eggs developed into rats with functional human genes.

Beginning 2 to 3 months after birth, the descendants of the transgenic rats spontaneously developed almost all of the symptoms of the spondyloarthropathies, including inflammation and destructive changes of the spine, large joints, bowel, skin and other organs. Principal investigators in this work were Dr. Joel D. Taurog at the Harold C. Simmons Arthritis Research Center at the University of Texas Southwestern Medical School in Dallas, and Dr. Robert E. Hammer in the Howard Hughes Medical Institute at Southwestern.

Future studies in which these transgenic rats will be bred and raised in a germfree setting may help investigators determine if an infectious agent is necessary to work with HLA-B27 in causing disease, as other studies have suggested.

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

NCI researchers Drs. Michael Gottesman (l) and Ira Pastan produced in 1989 a new line of genetically engineered mice that scientist say could help combat some chemotherapy-resistant cancers.

Modest Increases Characterize Budgets for 1991, 1992

By Calvin B. Baldwin, Jr.

The 1991 NIH Budget

Despite the furor over the federal budget deficit and the Gramm-Rudman-Hollings deficit reduction targets, NIH received a 9.2 percent increase in its budget for fiscal year 1991, as well as authority (in separate legislation) for the long sought-after Senior Biomedical Research Service. This new service will allow the Public Health Service to create up to 350 positions with salaries up to $138,900 to retain and attract biomedical scientists to its intramural laboratories.

On Nov. 5, 1990, the president signed into law H.R. 5257 (P.L. 101-517) making appropriations for the Departments of Labor, Health and Human Services, Education, and related agencies. This final appropriation was made after five separate resolutions had funded the federal government from Oct. 1, 1990, until all regular appropriations were signed.

The delay in enactment of regular appropriations bills was linked to passage of a budget reconciliation package, needed to satisfy the requirements of the Gramm-Rudman-Hollings Act with provision for increased revenues and changes in entitlement program expenditures. Until the latter measure was agreed to between the two houses of Congress and the White House, the appropriation bills were held up and there were threats of sequester and furloughs across the government. For NIH, furloughs were averted and for all government, sequestration was not invoked. However, this bill did include a 2.4 percent across-the-board reduction.

The following are highlights of the major provisions of the conference report (House Report 101-908) that address only the major differences between the House and Senate:

—The conference agreement provides $8,306,648,000 for NIH after the 2.41 percent reduction, a loss of $205,134,000. This is, however, a 9 percent, or $730.3 million, increase over the comparable FY 1990 level, and a 5 percent, or $378.7 million, increase over the FY 1991 request. Adjustments resulting from the reduction were directed to be spread uniformly across mechanisms, including research project grants.

—There is conference agreement that the "funds should be managed by the NIH consistent with the 4-year spending plan identified in the House and Senate reports accompanying the bill." It is expected that there will be no arbitrary downward negotiations of research grants with the funds provided, and a report is required within 30 days of enactment, giving precise estimates of the 1992-95 cost of implementing the plan.

—In addition, there was a $29.9 million reduction for NIH's share of a $50 million reduction in the amount appropriated to HHS for salaries and expenses, resulting in a 1991 net appropriation of $8,276,739,000 for NIH.

—Provision is made for a discretionary fund for the NIH director, both through a $20 million earmark in the Office of the Director account and a 1 percent transfer authority for the director.

—$15 million is provided for extramural construction grants, to be awarded competitively.

—Conference language gave specific directions to various NIH components as follows:

NCI: $7 million for proton beam therapy program; urging that $250,000 be used to initiate a study on tamoxifen in the prevention of breast cancer.

NHLBI: $8 million for the National

*(See **Budget** p. 12)*

The NIH Budget — FY 1991 & FY 1992

FY 1991 — Another good year for the NIH as Congress increases its budget 9.2 percent to $8.3 billion.

FY 1992 — President Bush requests $8.8 billion, a 6 percent increase over 1991.

(Budget Authority in millions)

	1989	1990	1991	1992	Change
Research Project Grants	$4,034	$4,180	$4,498	$4,893	+$395
(Number)	(20,681)	(20,281)	(21,186)	(21,818)	(+632)
Intramural Research	789	860	925	988	+63
Research Training	256	286	306	315	+9
Centers	605	633	713	746	+33
R&D Contracts	543	568	615	646	+31
Research and Management and Support	303	343	371	427	+56
Office of the Director	47	90	98	95	-3
Buildings & Facilities	38	61	169	104	-65
All Other	530	555	582	561	-21
Total, NIH	$7,145	$7,576	$8,277	$8,775	+$498
AIDS (non-add)	($602)	($742)	($804)	($851)	(+$46)
Full-time Equivalents	13,204	13,507	14,269	14,632	+363

Budget *(continued from p. 11)*

Marrow Donor Program (NMDP) for HLA typing, with an emphasis on recruiting minority groups underrepresented on the registry; $1.1 million for program administration of the NMDP; $3 million for an intramural bone marrow transplant unit at the NHLBI; the expectation that NHLBI will work with the Navy Medical and Research Development Command on the latter.

NIAID: Direction that pediatric AIDS trials be funded at the levels provided in the House report "less the proportionate reduction in the overall appropriation for the institute agreed to in conference."

NICHD: Funds included for second year of 5-year plan for research on sudden infant death syndrome, with expeditious implementation.

NIEHS: Additional $3 million for the National Toxicology Program, and $500,000 for academic awards for excellence in environmental and occupational medicine.

NIA: Sufficient funds to expand the health and environment survey and encouragement to support research on Alzheimer's disease prevalence in special populations.

NIDCD: Encouragement for support of neurobiology as part of the NIH celebration of the Decade of the Brain.

NLM: Expression of concern regarding potential changes in the Paperwork Reduction Act that would have an adverse impact on cost recovery and quality assurance efforts for the databases of the National Library of Medicine. It was stated that, should there be a change in the law, "strong consideration will be given to legislative action to restore current policies."

OD: $20 million for a director's reserve (in addition to the 1 percent transfer authority); urging expansion of extramural support for supercomputing through the National Center for Research Resources; $15 million for extramural construction; limitation on the 1 percent transfer authority to no more than 1 percent from any single appropriation.

Buildings/Facilities: $35 million to complete the Child Health/Neurosciences Building (Bldg. 49) and $60 million for the next phase of the Consolidated Office Building.

Office of the Secretary: Deletion of Senate language that would have fixed a 5-year term for the NIH director; new requirement for a Secretarial report to Congress, no later than Mar. 15, 1991, with a proposal for addressing the concerns regarding recruitment for the position and insulating it from political influence.

The 1992 NIH Budget

The president has requested $8,775,000,000 for NIH in FY 1992, an increase of 6 percent over FY 1991. The request emphasizes support for research project grants by providing $4.9 billion, an increase of 8.8 percent. The FY 1991 appropriations for NIH were accompanied by reports from the Congress that focused on the need for NIH to provide stable support for biomedical research. In FY 1992, NIH will support 21,818 research project grants, an all-time high for NIH. The training budget will support 12,318 research trainees, an increase of 140 awards over FY 1991.

A second area of emphasis in FY 1992 is the rehabilitation and renovation of NIH's research facilities, for which $104 million is requested. Together with funds appropriated in FY 1991, a total of $273 million will be devoted to this effort, which will fund crucial infrastructure improvements, the Clinical Center modernization/safety program, rehabilitation of older laboratory buildings, and renovations to NIH animal facilities. Ongoing construction projects include the Child Health/ Neurosciences Building, which is scheduled for completion by early 1992, and a new Consolidated Office Building, which received $58 million in FY 1991.

Specific research initiatives on which NIH will focus in FY 1992 include expanding efforts to map the human genome ($110 million), broadening the knowledge base on Alzheimer's disease ($209 million), and enhancing our understanding of and treatments for HIV/AIDS ($851 million).

The president's request for a 6 percent increase in NIH's 1992 budget must be viewed in light of his request for a 12 percent increase in government spending on research and development. The request for the National Science Foundation provides an 18 percent increase, and the budget for the National Aeronautics and Space Administration would grow by 13.6 percent. The Ad Hoc Group for Medical Research Funding, a coalition of 150 organizations, issued a statement that the proposed NIH budget would "fall substantially below the levels required to exploit the scientific opportunities that are currently apparent."

Baldwin was formerly NIH associate director for administration, 1980-86.

The 2nd NIH Alumni Day symposium sponsored by NHLBI will be held Monday morning, Sept. 23, 1991, in Masur Auditorium. We will have more details and information in our next newsletter.

The NIHAA would like to thank the Roche Institute of Molecular Biology for its generous contribution toward the publication of this issue of *Update*.

Gene Therapy *(continued from p. 1)*

Since 1986, Rosenberg has been treating certain cancers with TILs that have not been altered by gene insertion. About half the patients with advanced melanoma show some improvement after therapy with unaltered TILs.

"We need to improve TIL therapy, and one way may be with the addition of genes that can stimulate the production of antitumor toxins and thus enhance the ability of TILs to destroy tumor cells," Rosenberg said.

Dr. Steven A. Rosenberg

This trial, the first approved study using gene therapy to treat cancer, follows two earlier federally sanctioned trials with this new gene technology.

In a preliminary trial reported in the Aug. 30, 1990, *New England Journal of Medicine*, Rosenberg's team inserted gene-altered cells into patients with advanced melanoma, but the gene had no therapeutic potential. The inserted gene served only as a marker to identify TILs that could later be recovered from the patient's blood or biopsied tissue, thus helping scientists to better understand how these cells work in cancer therapy.

Last September, another NIH group—Drs. R. Michael Blaese and Kenneth W. Culver of NCI and gene therapy pioneer Dr. W. French Anderson of NHLBI—transfused a severely immunodeficient 4-year-old girl with her own white blood cells that had been altered in the laboratory by addition of the human ADA gene. The patient, who is doing very well so far, has ADA deficiency, an extremely rare, inherited disease that can result in death if untreated.

TNF is a protein produced by the body in the course of bacterial infections. Although initially recognized for its cancer-killing activity in mice, TNF also regulates inflammation and immunity by signaling the body to repair injuries and fight infection. However, if TNF is active in the body for too long or at too high a concentration, it can cause shock and body wasting.

At the tumor site, TNF appears to work by cutting off the developing blood supply in that region. By using TILs to target the tumor and carry the TNF gene directly to the tumor site, the scientists hope to maximize the gene's benefit and also minimize the potential toxicity that could result if TNF were distributed throughout the body.

"This gene therapy approach to cancer is being investigated in the research setting and is in an early stage of development," Rosenberg said. "Ultimately, it may be applied to a wide range of diseases, including cancers other than melanoma."

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

CALENDAR

MAY

An exhibit on "A Decade of Historical Acquisitions at the National Library of Medicine, 1981-1990" will be on display in the front lobby of the NLM (Bldg. 38, 8600 Rockville Pike) from May 1 through Aug. 30, 1991. The exhibit will highlight significant additions of the past 10 years to the collections of the library's History of Medicine Division. It will include rare books, manuscripts, prints, photographs, audiovisuals and ephemera. For more information call (301) 496-5405.

The R. E. Dyer Lecture will be Tuesday, May 7, 1991, at 3 p.m. in Masur Auditorium, Bldg. 10. The speaker will be Dr. Max Cooper.

The NIH Lecture will be Thursday, May 23, 1991, at 3 p.m. in Masur Auditorium, Bldg. 10. The speaker will be Dr. Wen-Hwa Lee.

NIHAA EVENTS

A "Mixer" sponsored by NIHAA at the AAP/ASCI/AFCR meetings, May 3-6, 1991, Seattle, Washington, will be held on Saturday, May 4, 1991, from 5 to 7 p.m. in the Madrona Room, Seattle Sheraton Hotel and Towers, 1400 Sixth Ave.

On Tuesday, May 21, 1991, from 7 to 9 p.m. the NIHAA will host a reception at the Embassy of Italy to honor the visiting Italian scientists at NIH. Details will be mailed to Washington area chapter members in mid-April.

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

Axelrod *(continued from p. 1)*

Axelrod was 33 when he began his research career and 43 before he earned a Ph.D. "Many (scientists) are over the hill by then," he laughs. Though he retired in 1984, he still works virtually every day, and has published some 35 papers since "retiring."

"People think I'm a sort of oddity," he admits. "I've had a very unconventional scientific career. I wouldn't recommend it."

Born in New York City 78 years ago, Axelrod remembers having been a voracious reader as a child. "I read a lot—I was intellectually interested in everything, and eager to learn."

Axelrod's first ambition was to become a doctor. He attended the free City College of New York, graduating with a B.S. in biology and chemistry in 1933. "I couldn't get into medical school, though, probably because of my religion. At that time, there were quotas for Jewish students in medical schools."

The year Axelrod graduated from college, the country was in the depths of the Great Depression and jobs were scarce. To assure that he could earn an income, Axelrod took the government's postal exam.

"I almost joined the Post Office, but a lab assistant job was open at NYU medical school, paying $25 a month," he recalls. "It was just pure luck that I decided to take the laboratory position."

After a few years in the lab, he obtained a job testing newly discovered vitamins in food at the Laboratory of Industrial Hygiene in New York.

"I was there for about 10 years," he remembers. "I didn't do research. My job was to modify existing methods for the analysis of vitamins to test in food products. The experience of developing and modifying methods proved useful in my subsequent research career."

Hardly anyone chose a research career in those days, Axelrod said. "There were few opportunities to do research and the work was poorly paid. What little work was done was supported by philanthropists. A person had to be wealthy and smart to do research. Few physicians did research in their spare time."

At this point, Axelrod still "had no idea of a research career." One day, the head of his laboratory—a retired professor of pharmacology named George Wallace—came to him with a problem: certain nonaspirin analgesics were causing blood disorders in some people. The professor advised that Axelrod see Dr. Bernard Beryl Brodie, who was on the faculty of NYU, about it.

"I met with Dr. Brodie one fateful day in February 1946," says Axelrod. "This was my first introduction to research. I found him to be a stimulating and inspiring person. He suggested that I join his lab to work on nonaspirin analgesics. We found that these compounds, acetanilide and phenacetin, formed toxic metabolites."

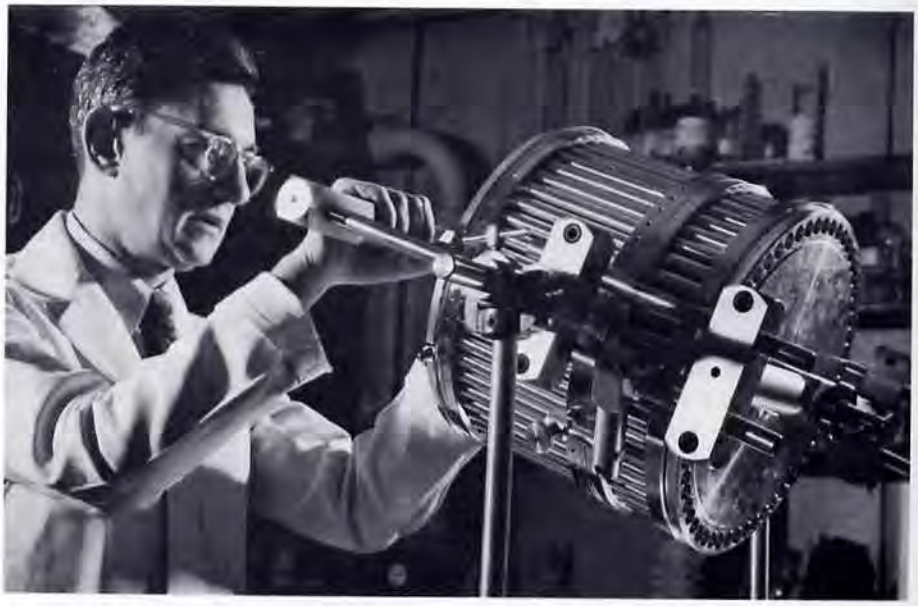
Curious to find what the main metabolites of these analgesics were, Axelrod and Brodie found that the drugs were metabolized to what is now known as acetaminophen. They also observed that this metabolite did wonders for headaches. Today, acetaminophen is known popularly as Tylenol.

"We didn't deliberately look for a new headache remedy," explains Axelrod. "It just turned up in the course of our research.

"I took to research immediately," he recalls fondly. "I did it well and I loved it."

Axelrod continued working in Brodie's laboratory at Goldwater Memorial Hospital (a branch of NYU medical school) and spent 3 years studying the metabolism of analgesics and anticoagulants. Realizing that he couldn't be promoted in academia without a Ph.D., he began a job search.

"One day I saw an item in the *New York Times* that James Shannon, formerly a professor at NYU medical



He was "Mr." Julius Axelrod when this picture—of fractionating equipment used in determining the fate of caffeine and other drugs and biologicals in the body—appeared in the Sept. 21, 1953, issue of the *NIH Record*.

school, was appointed head of the National Heart Institute," he said. "I wrote to him and he gave me a position at the heart institute."

Scientists were reluctant to come to NIH in those days, Axelrod remembers. "It was considered just another government lab. It was not at all as prestigious as it is today."

Axelrod credits Shannon, who became the eighth NIH director, with transforming NIH to the high status that it enjoys today.

"Shannon persuaded Congress that the way to treat and cure diseases is not to throw money at targeted research but to understand basic fundamentals of how the body works. He also had a great capacity to attract very good people."

At Shannon's bidding, Axelrod joined NHI in 1950, where he was reunited, at the GS-9 scientist level, with his mentor Brodie in the Laboratory of Chemical Pharmacology.

Located in Bldg. 3 on a campus that featured just a handful of buildings and about 100 employees, Axelrod found the atmosphere heady.

"It was a remarkable place," he remembers. "We were all young, and working in a very charged atmosphere. There were three future Nobel prize winners there—(Christian) Anfinsen and (Arthur) Kornberg were the others—and we all bumped into each other. There were also two eventual NIH directors (Drs. Donald Fredrickson and James Wyngaarden) and many investigators who became distinguished scientists.

"We were given a lot of freedom to do basic research, and the salary wasn't too bad. There was a critical mass of people," he reminisced. "We all knew each other and discussed each other's work.

"I was working fairly independently, and had published about 25 papers, including one on the discovery of a new class of enzymes that metabolized drugs, when I applied for a raise to a GS-12," he says, recalling an incident that still rankles him. "They turned me down because I didn't have a Ph.D."

Axelrod had earned a master's degree from NYU in 1941, which satisfied the classroom requirements for the Ph.D. he now began to earn at George Washington University. "I took a year of courses to pass the qualifying exams," he said. "My thesis was on enzyme work that I was doing at NIH."

Once he took his Ph.D. in 1955, Axelrod abandoned NHI for NIMH, where he spent the remainder of his career.

"I didn't quite get what I wanted at NHI, so I started a new career in neuroscience research," he states, simply. "I don't know whether you can do this today."

Axelrod's main research at NIMH was to study the chemistry of the nervous system, especially neurotransmitters.

"I did LSD research in the 1950's, and in 1960 described how cocaine and antidepressant drugs work (by blocking the uptake of catecholamines into nerves)," he said. "We were the first to get radioactive marijuana, and to show that it went into fat cells and stayed there for a long time."

The receptor for THC—marijuana's active ingredient—was cloned in his current lab chief Dr. Michael Brownstein's laboratory at NIMH, reports Axelrod.

Was he ever tempted to try any of the drugs? "I think you'd be crazy to do it. I've seen the bad things drugs can do," he says. "I get my kicks doing research."

Several of his colleagues experimented with LSD. "They said it distorted their perception of time and space," he said. "It was a little unpleasant."

*(See **Nobelist** p. 16)*

Axelrod (r) is surrounded by well-wishers including Dr. Roscoe Brady (l), Dr. Irwin Kopin (c) and Dr. Frederick Goodwin (r) when he learned of winning the 1970 Nobel Prize. Axelrod shared the prize in physiology or medicine with Bernard Katz and Ulf Von Euler "for their discoveries concerning the humoral transmitters in the nerve terminals and the mechanisms for their storage, release and inactivation."

Nobelist *(continued from p. 15)*

With the Shannon era, NIH's growing reputation began to attract more good people, Axelrod observes. "The Vietnam war also attracted a lot of bright M.D.s. Administrators had been very farsighted in getting the best people—like Kety (Dr. Seymour, head of NIMH) and Frederickson (who became NIH's 11th director)—and giving investigators the opportunity to select and carry out their own problems. We did great science.

"There wasn't the large bureaucracy there is now," he continues. "There were few regulations and restrictions on the kinds of experiments you could do. As the NIH grew, so did its bureaucratic infrastructure. In spite of this, I think the quality (of intramural NIH research) is really first rate.

"NIH still attracts top people," Axelrod allows, "but not as many as it used to. The very bright ones today go to top academic institutions. But most of the professors at those institutions are NIH-trained."

Axelrod says he'd think twice today about embarking on a research career: "I don't know if I'd want the hassle. But I love it so much that I would probably take the chance. Many prospective scientists are pretty cocky when they come out of college. Even if the grant funding level is down around 12-15 percent, you think you're good enough to get it."

Acknowledging that tenure at NIH is tough to get nowadays, Axelrod says it was easy three decades ago. "The corollary to that was that some dead wood accumulated," he said. "We used to have what was known as the 'NIH shunt'—scientists would gain their reputation at NIH and then leave for a professorship in academia."

Though courted by the private sector, Axelrod never thought seriously of leaving NIH. "I didn't want to go through the hassle of getting grants. My style of research was just a matter of following my nose. I could never predict where I might be 3 or 4 years down the road. At NIH, I didn't have to explain or justify to any great extent what I was going to do."

Which brings him to what he sees hampering young scientists today: "There is a tendency to do fashionable, safe research, to not take chances. If you take a chance and it doesn't work, it would be extremely difficult to obtain another grant. People tend to take on problems they know they can solve and do it just a little bit better than anyone else."

In spite of this, biological science, he admits, is growing at a tremendous pace.

"The important science is done by relatively few—maybe 10 or 20 percent—of scientists," he said. "Many just plod along, improving existing information. If one judges by literature citations, only 10 or 20 percent of the working scientists receive 80 to 90 percent of the citations."

"My style of research was just a matter of following my nose. I could never predict where I might be 3 or 4 years down the road. At NIH, I didn't have to explain or justify to any great extent what I was going to do."

—Dr. Julius Axelrod

Axelrod takes particular delight in acting as mentor to young scientists. "I always give advice. It's a great pleasure to work with and train young people," he says, eyes brightening. "I've trained about 70 people, many of whom are very distinguished."

Three NIH-Howard Hughes Medical Institute scholars are working or have worked in Axelrod's lab on the third floor of Bldg. 36, where he maintains a study stout with journals. Two intramural research directors—Dr. Steven Paul at NIMH and Dr. Irwin Kopin at NINDS—are his students. Other prominent academics, including Richard Wurtman at MIT and Solomon Snyder at Johns Hopkins, are also Axelrod alumni.

Axelrod's lab chief nowadays happens to be a former trainee—Dr. Michael Brownstein, whom Axelrod describes as "a sympathetic but tough guy—he has high standards."

Though he quit bench work about 10 years ago—"I don't think I'm good enough with my hands to do it anymore"—Axelrod continues to lecture and to exchange ideas with colleagues in his field. He can be amusingly offhand about his cogitations with his friends: "We talk about problems, we talk about ideas. Some work, some don't."

What continues to consume his still-curious intellect, however, is the chemistry of the brain.

"My main interest is neurotransmitters, the chemical signals of nerves. Neurotransmitters carry a special message to nerves and other cells. My colleagues and I are trying to find out how the neurotransmitter message is conveyed to the cell so that it can be stimulated to carry out a special function. This general area of research is called signal transduction."

For Axelrod, much of biomedicine, including immunology, cardiology, and the study of hormones and other chemosensory factors, involves transduction of biological signals. "Even the AIDS virus conveys a signal, but a bad one," he says.

"Signal transduction is a very complicated and fascinating field, one that we're just beginning to understand. Many clinical problems, including AIDS, diabetes, mental and cardiovascular disease, will be better understood by know-

ing how cells can send and interpret signals."

After 41 years here, Axelrod has a variety of opinions on the current state of NIH, which strikes him today as being "large, fragmented and very specialized. It's hard to know who's doing what, even in your own institute. Of course we're talking about a campus that is more than 10 times larger than it was when I first came." Other observations:

—On the genome project: "I think it's an important project, but I also think it's pretty boring. I don't know how getting the sequence of the genome will excite the very best scientists. One worry is that it would take money away from small science, where most of the novel ideas and advances come from. But you can't discount the possibility that the genome project would help small science."

—On RO1 (investigator-initiated) grants: "They are the guts of science. Any time you diminish that, you diminish the advance of science."

—On winning a Nobel prize: "We all dream of it, but I really didn't expect it. Once you get a Nobel prize, you become a sort of minor celebrity. It didn't change the way I did things at all. I didn't even have an office when I won the prize, only a desk in a lab."

—On fraud in science: "I think it's a minor problem. Misconduct generally comes out in the wash eventually."

—On retirement: "Unless you have a boring job, retirement is not a good thing. One of the ways one can stay young is to use your mind. My job is a labor of love and I find satisfaction doing it, even at this age. I manage to keep up with new advances. I retain some of what I read, but not everything. I feel very fortunate that NIH permits me to stay (he has a lab, two job slots and a budget). I don't work as hard as I used to. I also have the freedom to consult for biotechnology companies. I don't have to justify every little thing I do."

—On lab politics: "There are many styles of management in NIH labs. Some are very hierarchical and some are almost anarchistic. I would describe our lab as convivial. I like the style of freedom of interchange, and democratic decisionmaking. I think this freedom is the reason that American science has gone so far."

—On research careers: "The competition today is fierce but still worth the effort. There are a lot of disappointments in research. Most of the time your ideas don't work the way you want them to. But you forget about that and go onto the next thing. There is nothing as exhilarating as an experiment that turns out the way you hoped it would."

Though he admits to having bloomed late, Axelrod clearly believes in blooming long. "One can still do good work in the biological sciences at an advanced age," he noted.

His last observation, delivered with a self-deprecating chuckle, is about luck's role in a career that almost didn't happen: "I could easily have become a post office clerk."

'An Unexpected Life in Research'

Successful scientists are generally recognized at a young age. They go to the best schools on scholarships, receive their postdoctoral training fellowships at prestigious laboratories, and publish early. None of this happened to me.

My parents emigrated at the beginning of this century from Polish Galicia. They met and married in America, where they settled in the Lower East Side of New York, then a Jewish ghetto. My father, Isadore, was a basketmaker who sold flower baskets to merchants and grocers. I was born in 1912 in a tenement on East Houston Street in Manhattan.

I attended PS 22, a school built before the Civil War. Another student at that school before my time was I.I. Rabi, who later became a world-renowned physicist. After PS 22 I attended Seward Park High School. I really wanted to go to Stuyvesant, a high school for bright students, but my grades were not good enough. Seward Park High School had many famous graduates, mostly entertainers: Zero Mostel, Walter Matthau, and Tony Curtis. My real education was obtained at the Hamilton Fish Park Library, a block from my home. I was a voracious reader and read through several books a week—from Upton Sinclair, H.L. Mencken, and Tolstoy to pulp novels such as the Frank Merriwell and Nick Carter series.

After graduating from Seward Park High School, I attended New York University in the hope that it would give me a better chance to get into medical school. After a year my money ran out, and I transferred to the tuition-free City College of New York in 1930. City College was a proletarian Harvard, which subsequently graduated seven Nobel Laureates. I majored in biology and chemistry, but my best grades were in history, philosophy, and literature. Because I had to work after school, I did most of my studying during the subway trip to and from uptown City College. Studying in a crowded, noisy New York subway gave me considerable powers of concentration. When I graduated from City College, I applied to several medical schools but was not accepted by any.—**Julius Axelrod**

From "An Unexpected Life in Research," which Axelrod wrote for publication in the Annual Review of Pharmacology and Toxicology, 1988, 28:1-23.

Syphilis Research During a Decade of Discovery, 1900-1910; From Ignorance to 'Magic Bullets'

By Dr. Richard M. Krause

At the beginning of the 20th century, despite 20 years of intensive bacteriologic research, the cause of syphilis was unknown; no diagnostic test and no treatment had been found. Syphilis was one of the leading causes of morbidity and mortality. But success was soon to follow. In only 10 years, from 1900 to 1910, *Treponema pallidum* was discovered as the cause of syphilis. Animal models were developed for research. The Wassermann test was "invented" for serologic diagnosis. Paul Ehrlich developed Salversan, or 606, and proved that it was effective for the treatment of syphilis. This success was preceded by 300 failures with related arsenical compounds. As is the case with AIDS today, those who had syphilis were burdened with a social stigma. It was considered a disease of "bad blood." So the scientific, medical, social, ethical, and economic issues of that day have recurred again with the AIDS epidemic. The success, however, of Ehrlich, Wassermann, and others in the fight against syphilis is an optimistic omen that researchers will be equally successful in the fight against AIDS.

How serious was the syphilis epidemic in the first decade of this century? In Paris alone, 3,000 people died each year from the late stages of syphilis. At least one-third of patients committed to mental institutions had paresis.

Animal Models

For 20 years after Koch's discovery of the tubercle bacillus, efforts to identify the cause of syphilis and to transmit the disease to animals failed. In 1905 in Padua a former student of Ehrlich's produced syphilitic inflammation in the anterior chamber of the rabbit eye. Shortly thereafter, two Italians produced syphilis in the scrotum of rabbits, a model used to this day. These animal models were needed to study the effects of experimental drugs for syphilis before their use in humans. Two years later at the Dermatology Clinic at the Charité in Berlin, Fritz Schaudinn and Erich Hoffmann detected the causative organism of syphilis in the serous fluid of chancre lesions.

Paul Ehrlich and Development of Salvarsan

In the first decade of this century, Paul Ehrlich was becoming somewhat disenchanted with specific immune serum therapy and the slow pace of vaccine development for meningitis, typhoid, tuberculosis and other infections. He turned increasingly, therefore, to the idea of developing chemical "magic bullets," or drugs, to augment the body's own natural "bullets."

Dr. Paul Ehrlich

Sometime around 1906, Ehrlich began his research with arsenic compounds in an attempt to find a treatment for syphilis. This finally led to compound 606 or Salvarsan. By 1909, in 3 short years, Salvarsan had been produced and tested in animals and then in humans. Think of the task: synthesizing 300 different yet related arsenic compounds, numbered 306 to 606, and conducting animal experiments on each to determine efficacy and toxicity. In those days, and certainly even today, it was a tremendous endeavor. Ehrlich's notebooks reveal that progress was slow and difficult. For example, in his entry describing the use of compound 418 in animal experiments Ehrlich wrote, "I am fully aware that the initial animal experiments allow no conclusions about therapy of human subjects."

There was little reason to anticipate success with the synthesis of compound 606 at the end of May 1909. The epochal experiment with compound 606 to treat syphilitic keratitis in rabbits was conducted on June 8, 1909. The inflamed cornea healed rapidly, which was the first time such a result was achieved. On June 23, compound 606 was used to cure rabbits with syphilis of the scrotal sac.

During the summer of 1909, Phase I clinical trials were begun in humans. What would be the benefits? How serious would be the toxic side effects? The chemical firm, Hoechst, scaled up to manufacture the drug. By September, 23 patients with advanced syphilis, the majority of whom were paralytics, had been treated. Ehrlich did not expect that patients with tertiary syphilis would show significant improvement. But two of the patients developed negative Wassermann blood tests, and several had a decline in positive values. That change was remarkable. Previous clinical experience had shown that positive blood tests always persisted in patients with tertiary lues.

The next step required larger clinical trials. The results exceeded expectations. Syphilis, particularly in its early stages, was treated successfully with Salvarsan, and there was reason to believe that pa-

tients would not develop the late, fatal complications of syphilis, such as heart disease and paresis.

Both the general public and the medical profession were extravagant with their praise for Paul Ehrlich and Salvarsan. Their enthusiasm was understandable, because syphilis, like AIDS today, was no ordinary disease. There was the fear concerning the terrible, fatal course of syphilis—paresis, tabes, heart disease. There was the additional anguish stemming from the social disgrace. Syphilis was the disease of "bad blood." Hence, anything that was new about syphilis made the daily newspapers, just as AIDS does today.

As the evidence became more and more convincing that Salvarsan was an effective drug for the treatment of syphilis, issues of supply and cost became matters of public controversy. By November 1910, Hoechst was repeatedly accused in the press of delaying the supply of Salvarsan for profit motives, and Ehrlich himself was drawn into this harsh and bitter controversy. Today there is similar controversy over the high cost of AZT for the treatment of AIDS.

The Wassermann Reaction: A Diagnostic Blood Test for Syphilis

The Wassermann blood test to detect syphilis was developed by a long and circuitous route of trial and error, blind alleys, and mysterious serological procedures. It was a messy business, with little of the elegance of Ehrlich's search for the magic bullets. The history of the Wassermann reaction was told by Ludwik Fleck, a Polish physician, microbiologist, immunologist, and philosopher of science, in a book entitled, *Genesis and Development of a Scientific Fact*.

"The procedure is based on five little-known factors, whose mutual effects are adjusted by means of preliminary tests and whose mode of application is secured through a system of controls...the experienced eye or the serological touch is much more important than the protocol. It is possible to obtain a positive Wassermann reaction from a normal blood sample and a negative one from a syphilitic sample without any major technical errors...and yet the optimum intermediate position between minimum nonspecificity and maximum sensitivity was gradually established."

Dr. Richard M. Krause

Doesn't that sound familiar in regard to AIDS serology—those twins, specificity and sensitivity?

By 1930, there were at least 8,000 published scientific papers on the Wassermann reaction, all of which were done before the NIH awarded research grants! What an army of serologists that effort took, most of whom are unknown to us today.

In his historical review of the Wassermann reaction, Fleck examined the real nature of scientific discovery. He gave fair warning to those who believe that science is more scientific than it really is. Scientists and the public must be fully aware of the unpredictable nature of our search for discovery. Fleck said "an important discovery was made after many errors and detours from false assumptions and irreproducible initial experiments." We should remember the history of the Wassermann reaction when we write a grant application and when we review a grant application. We must avoid the safe, the doctrinaire, the predictable, and the fashionable.

Conclusion

For those working on AIDS today, there are lessons to be learned from this history of Ehrlich, Wassermann, and Fleck and their work on syphilis. No one person developed and perfected the Wassermann reaction. It was the work of a *Denkkollektiv*, Fleck's term, a "thought collective" of scientists. Progress comes through their collective efforts. No one person is going to solve the AIDS problem or even one aspect of it. Even Ehrlich was a member of a *Denkkollektiv*.

We will develop a more reliable diagnostic blood test for AIDS than we now have. We will learn how to use it and interpret the results. In addition, I have no doubt we will develop more effective drugs to treat AIDS, at least in its early stages. This may mean treatment at the time of the initial asymptomatic infection, as detected by seroconversion, just as is done today with tuberculosis.

Commenting on his success with experimental chemotherapy, Ehrlich noted that his four big G's played an important role: "*Geduld, Geshick, Gluck*, and last but not least, *Geld*." Patience, skill, luck, *and money*. Scientists who are confronting the perplexing pathogenic processes of AIDS and its complex natural history, in an effort to devise methods of treatment and prevention, should remember Ehrlich's four G's. These four G's were the currency that purchased the remarkable advances from ignorance to magic bullets for the treatment of syphilis during the decade of discovery, from 1900 to 1910. Success in the fight against AIDS will be bought with the same coinage.

Dr. Krause is Senior Scientific Advisor, Fogarty International Center, National Institutes of Health.

Human Genome Project Meets Its Market

By Rich McManus

The National Center for Human Genome Research held a briefing on the human genome project recently for a variety of voluntary health associations representing patients and families with inherited diseases—in short, the consumers of new genetic technologies.

Guests learned that investigations of DNA's double helix wind through every institute and illness at NIH, not just at NCHGR. "Genome research is not just a separate entity," reported Dr. William Raub, NIH acting director.

The human genome project "is the molecular genetics of man conducted in a cost-saving and very accelerated manner," explained Dr. C. Thomas Caskey, who heads an NCHGR-supported center for genome research at Baylor College of Medicine. "It would take 100 years to accomplish without the project, but with it it should last about 15 years.

"Americans are impatient about progress," he observed. "We like to see technology pushed as fast as possible."

Caskey, who is also president of the American Society of Human Genetics, called the project "an international, peaceful and scientific initiative. We are going to learn about ourselves at a molecular level."

What we learn will be "inseparable nation to nation, people to people, and will encompass many religions, social contexts, and governments. It will provide fuel for biology for the next 20 to 50 years."

The program will give researchers tools to answer two simple questions, he said: How do genes work? How do genes go awry?

"We need to learn how to modify the pathologic pathway," he said.

Mammals, Caskey explained, have genes scattered along their chromosomes, which makes their function hard to understand. "If we know where a particular gene resides, then we can find and isolate it," he said.

Reviewing technological progress in recent decades, Caskey described an ever-finer set of lenses through which we view genes, culminating in the latest technology of sequence tandem base-pair repeats, which allow "a precise roadmap—very dense—which can put genes in precise positions on the map."

A tenfold increase in resolving power has been realized in recent years, with prospects for even finer resolution quite likely.

Not just human, but also mouse, yeast and E. coli genomes are coming under scrutiny as scientists try to perceive principles of organization of chromosomes and location of genes. Whereas human DNA consists of only about 1 percent coded sequences, DNA from yeast and E. coli contains almost 100 percent coded sequences, Caskey said. Comparison studies, increasingly easy to carry out, should yield more information about how genes function.

Dr. Nancy S. Wexler

"There are a large number of diseases that have genetic bases but are not necessarily heritable or linked to one gene," Caskey continued. Such phenomena as aging, diabetes mellitus, coronary artery disease and cancer are the result of many factors, not only genes. Understanding the interaction of the environment and nature will help tell us who we are, said NIH's Raub.

Offering the perspective of an actual gene hunter was Dr. David Housman, a molecular biologist at MIT who for the past 12 years has studied hemoglobin genes, eventually identifying the gene for Wilms' tumor.

"We're more like gene chasers," he modified, before offering a tour of his research "scrapbook" that was designed to answer the question, "How does a researcher pick a chromosome to study?"

"The genome looks like a series of doorways," he said, "behind which is something unknown. The number of doors we have to open will differ with each disease, but the human genome project will give us the tools to open those doors." Housman said the order of the metaphorical doors is similar across species, from mice to humans. In the 10 years since gene mapping became possible, the easy challenges have fallen first, he said. "The process so far has taught us what the hard parts are that lie ahead."

Dr. Nancy S. Wexler, who chairs the joint NIH-Department of Energy working group on ethical, legal and social issues, claimed a personal stake in genetic research—she comes from a family affected by Huntington's disease.

"We're in a very dangerous period," she said, "when we can detect the defective gene but can't treat the diseases that the bad genes cause."

Finding disease genes will be a long, uphill struggle with many false leads, she cautioned, but urged the program to go forward nonetheless.

"Just knowing a disease gene—like the sickle cell gene, which we know back and forth—isn't going to lead to a pana-

cea in the next half hour," she said. "Getting the gene isn't the same as getting the cure, but it's well worth our while to look for them."

Adding a further note of caution was Dr. Robert F. Murray Jr. of Howard University, who also serves on Wexler's working group. "To screen or not to screen, that is the question," he began. A bittersweet review of the history of sickle cell anemia screening in the United States—during which such groups as the Black Panthers and professional baseball players added their dubious authority to the confusion about the disease—led Murray to his conclusion: "There is no end to the absurdities that screening (for genetic diseases) will engender. If you can imagine (a worst case), it will happen. If you don't believe me, just tune in to the Donahue show or Oprah Winfrey."

To prevent, or circumvent, the sort of disasters foreseen by Murray, the NCHGR is spending 3-5 percent of its budget trying to harness the social, rather than medical, power of genetic information through its Ethical, Legal and Social Implications Program.

Headed by Dr. Eric Juengst, the program has three aims: anticipate dilemmas engendered by genetic testing, develop policy options to safeguard society against abuses of genetic information, and educate the public and the profession about what genome research can and cannot offer. "What is fair when it comes to gathering genetic risk information about other people?" Juengst asked. "How good are protections against genetic discrimination?"

Juengst's program is focussing mainly on insurers and employers, as many are concerned that insurance companies will use genetic screening to refuse coverage to workers.

"Will insurance companies regard pre-symptomatic test diagnosis as a prior existing condition (and thus refuse to offer coverage)?" wondered Caskey. "The truth is, everybody has a (genetic) predisposition to something."

Wexler said the genome project is forcing insurance companies to rethink the way they do business. A two-edged sword, testing can spur the genetically "fit" to drop coverage while prompting those with weaknesses to buy more.

Since the prospect that genetic information might be misused to create "perfect" people is a major concern of consumers of new genetic technologies, NCHGR deputy director Dr. Elke Jordan concluded with an anecdote that was both seasonal and instructive.

A company that offered specially bred Christmas trees with absolutely perfect shape and symmetry, she explained, found, to its consternation, that the public doesn't care much for perfection—imperfect trees with "character" were actually preferred.

Editors Loosen Grip on Medical News

By Rich McManus

Editors at two of the nation's most prestigious medical journals concede that certain medical news is too important to hold for the printed page and may be disseminated by other means prior to actual publication. One channel suggested for early distribution was Medline, NLM's online access to citations in medical literature. Such availability would not jeopardize publication of the article at a later date.

"An approved manuscript could be released online through the National Library of Medicine before actual publication," said Dr. Arnold Relman, the recently retired editor of the *New England Journal of Medicine*.

Dr. George Lundberg, editor of *JAMA*, allowed that there will be times when medical breakthroughs slated to appear in one of the 10 AMA journals may be released prior to publication. Such early dissemination could precede publication by anywhere from 3 to 8 weeks.

The two rival editors provided most of the fireworks at a workshop convened at NIH to discuss dissemination of clinical trial results. Both paid homage to the painstaking care necessary to conduct such trials, and to the necessity of unsparing peer review. But in the end, both agreed that physicians, being the primary users of such information, and patients, being the primary beneficiaries of their enterprise, need to know about new treatments in the swiftest way possible, even if it means that journals will be "scooped."

While such flexibility has rarely been the rule so far, editors and physicians must now decide when a study's results are so important that prepublication release of information is warranted. Dr. William Raub, NIH acting director, has asked a top-level committee of NIH officials to consider when such measures are appropriate.

"For most studies, regular peer review with no details released prior to publication is best," said Relman. "This allows for quality control, limits mistakes, minimizes the hype, exaggeration and bias, and prevents premature and unwarranted conclusions. In the great majority of circumstances, short-circuiting this process is not a good idea.

"Most new clinical information doesn't come with a big bang," he continued. "It's a gradual process. Publication should be slow, deliberate, critical, discerning and conservative—in short, it should be consistent with the way the data were collected.

"Occasionally there is a great rush, when we need a faster but no less reliable way of completing this process," he said. "We will set aside our embargo and the Ingelfinger rule (named after his predecessor as editor-in-chief and limiting

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Editors *(continued from p. 21)*

NEJM articles to those not previously announced in any other media) when the news is of urgent importance."

Relman also said NEJM will publish work that has been previewed in a "clinical alert" (put out by NIH information offices to get the word to practitioners) or abstracted on electronic bulletin boards.

"I don't think there's a basic problem here," said Relman, who was the first of several speakers on the 18-person panel to understate the problem. "The system as it stands is good, but may need some fine tuning."

Echoing his reserve was NLM director Dr. Donald A.B. Lindberg, who views the library as a logical choice for speedy dissemination of research results.

"We're not in the business of producing Holy Writ," he remarked. "We're not claiming that (articles previewed in Medline) are all true. We do try hard, however, to get it accurate, timely, and in a form people can use."

Panelists discussed six examples of trials where results were unusually consequential. In each instance, the parties in the process—researcher, editor, reporter and patient (not to mention funding agency)—have agendas that may not be in consonance with the others.

"There is no NIH policy for dissemination of trial results as yet," said Dr. John Ferguson, who heads NIH's Office of Medical Applications of Research, which cosponsored the meeting. "This is a first step."

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FAES Offers Graduate School at NIH

The Foundation for Advanced Education in the Sciences (FAES) Graduate School was initiated in 1952 to provide continuing educational opportunities to NIH scientists. In the 1990-91 school year, about 2,400 registrations were recorded in 170 courses. Evening courses are offered at college, graduate and postgraduate levels in many areas: biochemistry, biology, biophysics, chemistry, communications, computer sciences, general sciences, genetics, immunology, management, mathematics, medicine, microbiology, modern languages, pharmacology, physics, physiology, psychiatry, psychology, social sciences, statistics, toxicology, and virology as well as a few courses in the arts and humanities. A series of medical subspecialty review courses and postgraduate medical courses are offered, all of which are approved for credit in Category 1 of the Physician's Recognition Award of the American Medical Association.

A majority of the school faculty comes from the NIH staff; the large scientific population at NIH contains many investigators and administrators with a strong desire to teach. Advanced courses are presented by scientists with particular competence and experience in specialty areas.

Courses are approved by the Maryland Higher Education Commission, and are generally accepted for degree credit by universities throughout the world. Introductory and intermediate level courses are of great value to technical personnel seeking to expand their capabilities and backgrounds, and are considered by the Office of Personnel Management for promotion or reclassification purposes. Many of the students already have an M.D. or Ph.D. degree and take advanced courses to broaden their knowledge in specialty areas or to review and update.

Although initiated primarily for NIH staff as the students, the FAES Graduate School is open to the public. Presently, almost half the enrollment comes from outside NIH (from other federal and municipal agencies, local universities and from the community at large). The courses in continuing medical education are particularly valuable to practicing physicians in the Washington area, because they are held in the evening. Through its Graduate School, the FAES provides needed educational opportunities to scientists, physicians, nurses and students from NIH and the entire Washington area.

The school is constantly in need of instructors and organizers for existing or new courses. Such an activity is ideal for the retired scientist or administrator, not only as a way to remain involved but also as an opportunity to pass on one's wisdom and experience to new generations; there is even a modest remuneration for the effort. If you are not familiar with the school, you can obtain a current catalog by calling (301) 496-7976.

Anyone who has the appropriate background, and would like to participate in the teaching and/or organizing of existing courses or even in creating new ones, is invited to contact Lois Kochanski at (301) 496-7976 or write to FAES, One Cloister Court, Bethesda, MD 20814-1460.

You will be soon receiving a dues renewal notice from NIHAA. Please return it promptly. Dues are an important source of our income and we need your continued support.

Children's Inn at NIH Burgeons in First Year

By Anne Barber

Since July 2, 1990, when the Children's Inn at NIH opened, more than 475 patients and their families from 44 states and 8 foreign countries have stayed in this NIH residence. The children have come to the inn through referral from 10 of the 13 NIH institutes.

"In addition to the heartwarming support we've received from the Clinical Center's medical team and the social workers who are the source of referral for our residents, we have been blessed with help from the entire NIH community. From groundskeeping to emergencies involving the police, transportation services, fire, safety and maintenance services—all have taken extra care of the Children's Inn, and we are most grateful," says Andrew Tartler, executive director of the inn.

"All the hard work put into the design and establishment of the inn has paid off. Our family-centered, self-help concept has been fully realized when you look at the excellent use patients and their families have made of this facility."

When the inn first opened, there were four full-time staff members: Tartler; Kate Higgins, resident manager; Pam Keller, director of volunteers; and Zulienne Wolfrey, administrative assistant. Since then, the board has hired two additional staff members: Margo Bradford, day manager, and Jean Buergler, bookkeeper.

Bradford, who shares the managerial load with Higgins, says, "Our intake has steadily increased so that we have had to implement an administrative/medical priority system to decide who to admit. The inn can provide for up to 36 families, but when we are full, we have procedures to determine who stays and who doesn't, based on the child's health. Many nights this month (January), we have been full."

A significant strength of the Children's Inn is its volunteer corps. There are currently 150 volunteers serving the inn. They range, according to Keller, from ages 16 to 70 years, and include working people as well as the retired.

"We have varying degrees of commitment from our volunteers—from people who bake for parties to our weekend volunteer resident managers. We provide staffing 7 days a week, for approximately 1,500 volunteer hours a month."

Except for the contract cleaning service, volunteers do everything that is required to keep house. They replenish kitchen supplies, pick up the playroom, make sure fresh linens are placed in each linen closet, fill bird feeders. They also work at the welcome desk answering phones, accepting and orienting patients and their families, ordering the shuttle van, arranging monthly tours of the inn, and taking residents to the grocery store.

Keller was swamped with calls from potential volunteers even before the inn opened. "In fact," she says, "I received so many I had to limit them to one shift a week.

"The only trouble we had was getting people to come and stay over a weekend. Once we advertised the need, we received adequate weekend and holiday volunteer coverage."

Volunteers make grocery trips with residents four times a week and they drive the inn's van during the weekend when the NIH shuttle doesn't provide service to the Clinical Center and the Metro station.

Tartler emphasizes, "The NIH community has responded very generously to our needs for volunteer help."

Keller says she gets many calls from people wanting to do things for the inn. "For example, as early as last summer, the NIH firemen came to me and offered to do a holiday party for the children in

*(See **Inn** p. 24)*

In the lobby of the Children's Inn at NIH, children play in front of a dollhouse donated by William B. Edelblut Jr. of O'Donnell's Restaurant Inc. Volunteers Wendy and Joseph Allan restored the dollhouse to its original splendor.

Inn (continued from p. 23)

December. We agreed, they did, and it was a big success."

"The dream," says Tartler, "that the Children's Inn would become a national model has become more and more true. We continue to reap the benefits of national recognition because of the type of service we provide here. Some of this may result from having been on the *Today* show twice.

"As we continue to meet the ongoing needs," he says, "our 'wish list' continues to grow."

Tartler mentions the number one priority—automatic doors for the two sets of front doors and the residents' evening access door.

"Also, we would like to develop the exterior of the property to match the beauty of the interior. We would like a special playground, barbeque grills, picnic tables, a gazebo, park benches, plantings, as well as wildlife feeding stations.

"These kids," he says, "spend weeks and months inside institutions, so we would like to provide them with an opportunity to spend some time outside. We are in the planning stages now, and estimate the cost to be around $118,000."

On Feb. 7, a board change at the inn took place. The original two boards—operating and fund development— merged into one board of directors. The new board, consisting of 25 members, is responsible for establishing an endowment fund that will provide the inn with annual operating expenses.

Tartler says NIH contributes laundry service, maintenance, utilities, and shuttle service, in addition to the land it has already given. However, funds for operating costs are required to support the inn, hence the need for an endowment fund.

"Outside generosity to the inn has been most gratifying," Tartler reports.

A-Wing Addition Rises on East Side of Bldg. 10

By Rich McManus

A major addition is currently being grafted atop the four existing floors of Bldg. 10's A wing; the $11 million fast-track project, due for completion in fall 1991, will add new NCI and NIAID laboratories to the fight against AIDS.

The first of two construction phases—erection of the steel superstructure—began last March and will soon be completed. Phase two has just begun and will result in state-of-the-art laboratories whose flexibility and space are unequaled in the Clinical Center.

"It's pretty hard to start a construction project four stories up from the ground," said Donald A. Sebastian, the project officer for the Division of Engineering Services who is overseeing completion of the wing's first phase. "It's a very intricate, exacting type of construction—we call it our Swiss watch.

"The whole project, from design of the addition to finished construction, will take a little more than 2 years," he continued. "For a job of this size and intricacy, that's pretty fast."

The B1, B2, first and second floors of the existing A wing will remain unchanged, aside from some work to the loading dock area. The roof of the current A wing will become mechanical or "interstitial" space, allowing for pipes and ducts. The next three stories will align with existing floors in the adjacent B wing and will be worker-occupied. The top floor will be entirely devoted to mechanical space.

The first usable floor of the addition will be utilized for office space divided in thirds for NCI, NIAID and the assistant hospital administrators from the CC.

The next two floors—comprising some 11,000 square-feet each and including 28 laboratories of single, double and triple modular configuration with their necessary support—will be occupied by NCI and NIAID labs.

These two floors can each accommo-

The steel superstructure of the new AIDS Research Facility atop the Bldg. 10 A wing is now complete. Two of the addition's floors will include NCI and NIAID laboratories dedicated to research on human immunodeficiency virus.

date 33-35 single modules, each 11 feet wide. About one quarter of these will operate as biosafety level 3 (BL3) laboratories, needed for some retrovirus procedures. In these labs, workers must enter via an anteroom instead of directly from the corridor; in some cases, material exiting the labs must traverse a pass-through sterilizer. The remaining modules will be biosafety level 2 (BL2) labs, which can be entered directly from the corridor, and can be easily converted to BL3 labs if the need arises in the future.

Most-Cited Women in Science Have NIH Ties

By N. Sue Meadows

Eight of the 10 women recently identified by the Philadelphia-based Institute for Scientific Information (ISI) as the most-cited women in science have received NIH research grants and have served as reviewers for the NIH peer review system. Three of these scientists are supported by an NIH MERIT Award, which provides extended support to foster the continued research achievements of distinguished scientists. At least two have worked in the intramural labs on the NIH campus.

According to the ISI, the list of the 10 most frequently cited women in science was compiled from the files of ISI's *Science Citation Index* through a computer study that counted how often each scientist's published work had been cited in articles written by other scientists.

The scientist most cited was Dr. Flossie Wong-Staal, who is an NIAID and NCI-supported researcher at the University of California, San Diego, and was previously at NIH as an intramural scientist in NCI's Laboratory of Tumor Cell Biology. Her work was cited by other authors 7,772 times from 1981 to 1988. Her most-cited paper is "Human T-lymphotrophic retroviruses," published in the British journal *Nature* in 1985.

In addition to receiving NIH research support, Wong-Staal has served as a peer reviewer for DRG's AIDS and related research-3 study section during the June 1989 round of initial review. Also, she is a member of the NIH reviewers reserve, a centralized file of consultant reviewers available to all NIH chartered scientific review committees to assist in the peer review of grant and cooperative agreement applications and contract proposals.

The third most-cited scientist is Dr. Philippa C. Marrack, an immunologist who works in molecular biology at the National Jewish Center for Immunology and Respiratory Medicine in Denver, whose work has been cited 6,462 times. She served as a member of DRG's immunobiology study section from July 1980 to June 1984, and has received research grant support from NIAID.

Three of the 10 scientists, Drs. Mary Jane Osborn of the University of Connecticut Health Center, Joan A. Steitz of Yale University, and Marilyn S. Kozak of the University of Medicine and Dentistry, Newark, N.J.(UMDNJ), have provided expertise to DRG's molecular biology study section in the initial review of grant applications. Osborn, whose work was cited 4,366 times, is currently a member of the DRG advisory committee. She has also served on the National Advisory General Medical Sciences Council and the Board of Scientific Counselors of NHLBI. She has grant support from NIGMS and NIAID.

Steitz, a biochemist at Yale and a Howard Hughes Medical Institute investigator, has 3,282 citations for her articles. She is an NIGMS-supported MERIT awardee and has received grant support from NCI and NIAID as well. From 1976 to 1980 she served on the NIADDK Board of Scientific Counselors.

Kozak, who studies messenger RNA and eukaryotes (cells with nuclei), has 3,107 citations to her credit. Besides currently serving as a DRG study section member, she is an NIAID and NIGMS-supported investigator at the Robert Wood Johnson Medical School, UMDNJ.

Dr. Ellen S. Vitetta, who helped discover immunotoxins and whose work has been cited 3,098 times, is an NCI MERIT award recipient. Her most-cited paper, "Cell surface immunoglobulin II: Isolation and characterization of immunoglobulin from mouse splenic lymphocytes," was published in the *Journal of Experimental Medicine* and is 19 years old. A scientist at the University of Texas Southwestern Medical Center, Dallas, she has also received grant support from NIAID and served as a reviewer for DRG.

Dr. Candace B. Pert is a former intramural scientist with the National Institute of Mental Health who in the 1970's helped identify natural pain killers produced by the brain. Her work has been cited 2,918 times. She has received grant support from NCI and NIGMS of NIH, and NIDA of ADAMHA. She was a member of DRG's neurology B study section from 1981 to 1984.

Dr. Marilyn Gist Farquhar, a researcher at the University of California, San Diego, who studies cell biology and experimental pathology, was the ninth most-cited with 2,316 citations. She is an NIDDK supported MERIT award recipient and also has received support from NCI and NIGMS. She has served on two DRG study sections: cellular biology and physiology from 1975 to 1979, and pathobiochemistry from 1986 to 1990.

The remaining two members of the 10 women of science, Drs. Julia Margaret Polak of Hammersmith Hospital and Sheila Sherlock of the Royal Free Hospital, are researchers in London, England, and have not served on NIH peer review committees nor received NIH grant support.

NIH Notes for November 1990— February 1991

HONORS AND AWARDS

Dr. Robert M. Chanock, chief of NIAID's Laboratory of Infectious Diseases, was selected winner of the 1990 ICN International Prize in Virology. The annual prize, an engraved crystal prism and $50,000 in cash, honors his career and work during the last 35 years including discovery of several medically important viruses, research on infectious viruses especially in childhood diseases, and work in vaccine development ... **Dr. Igor Dawid,** chief of NICHD's Laboratory of Molecular Genetics, received the Distinguished Presidential Rank Award for his "pioneering research accomplishments in developmental biology and molecular genetics leading to new approaches to the cure of gene disorders" ... **Robert T. Dillon,** assistant director for policy and evaluation in the Division of Personnel Management, OD, received the All Star Team Award from the federal section of the International Personnel Management Association for his leadership in designing and implementing the new pay program; and for his contributions to NIH efforts to obtain legislative approval of a pay and personnel system for senior scientists ... **Dr. Cheng Dong** of the Biomedical Engineering and Instrumentation Program, NCRR, received the 1990 Melville Medal of the American Society of Mechanical Engineers as first author of the best original paper presented for discussion and publication: "Passive Deformation Analysis of Human Leukocytes" ... **Dr. Charles H. Evans,** chief of the tumor biology section in NCI's Laboratory of Biology and a captain in PHS, was awarded at the 9th annual meeting of the Association of Military Surgeons the Sir Henry S. Wellcome Medal and Prize for his essay on "Leukoregulin: A New Biotherapeutic Cytokine in the Search for More Effective Antiviral Pharmacologic Agents" ... **Evelyn Farinas,** supervisor of Oncology Pharmacy, Clinical Center, won the Hospital Pharmacist of the Year award for 1990 from the D.C. Society of Hospital Pharmacists. Last year's winner, Karim Calis, is also a CC Pharmacy employee ... **Dr. Anthony S. Fauci,** NIAID director, received the First International Chiron Prize for Biomedical Research during a ceremony in Rome, Italy. He also received the degree of doctor of medicine and surgery, honoris causa, from the Universita di Roma, "La Sapienza," in Rome. He also became the 17th recipient of the "Presidential Award of the New York Academy of Sciences, Supported by A. Cressy Morrison," for his "outstanding accomplishments in science and service in the cause of science" ... **Stephen A. Ficca,** director of NHLBI's Office of Administrative Management, received the Meritorious Presidential Rank Award "for outstanding leadership and initiative which have made significant contributions to the improved management of the programs at the National Institutes of Health" ... **Dr. Robert C. Gallo,** chief of NCI's Laboratory of Tumor Cell Biology, recently shared the 1990 Karl Landsteiner Memorial Award with Dr. Luc Montagnier of the Pasteur Institute; the scientists were honored at the joint meeting of the American Association of Blood Banks and the International Society of Blood Transfusion in Los Angeles. Gallo also recently gave the following distinguished lectures: the 19th Maxwell Finland Lecture at the annual meeting of the Infectious Diseases Society of America held in Atlanta; the Yuri Ovchinnikov Memorial Lecture at the Shemyakin Institute of Bioorganic Chemistry in Moscow; the Shell Lecture at Oxford University; and the Sir William Osler

Drs. Robert C. Gallo (l) and Luc Montagnier (r) received the AABB 1990 Karl Landsteiner Award, which was presented by AABB president Toby L. Simon.

Lecture at McGill University. He also delivered the Luther Terry Lecture at the U.S. Public Health Service Professional Association meeting in Anchorage ... **Dr. Alfred G. Gilman,** an NIGMS grantee, recently received the 1990 Steven C. Beering Award for his outstanding achievement in biomedical science. The $10,000 award is given annually by Indiana University ... **Dr. Fann Harding,** assistant to the director of the Division of Blood Diseases and Resources, NHLBI, was awarded the American Association of Blood Banks Distinguished Service Award in recognition of her leadership in initiating and establishing the Transfusion Medicine Academic Awards program and maintaining it as a major force in transforming transfusion medicine ... **Dr. David I. Hoult,** who heads the nuclear magnetic resonance instrumentation group in the Biomedical Engineering and Instrumentation Program, NCRR, is the first recipient of the Award for Achievements in the Field of Magnetic Resonance for "his invention of rotating frame imaging and his many innovations in NMR probes, receivers, magnets, and computational procedures which have had widespread impact on the field" ... **Dr. Carl Kupfer,** NEI director, received the Distinguished Rank Award "for sustained extraordinary accomplishment in planning, developing, and managing a nationally and internationally acclaimed vision research program" ... **L. Earl Laurence,** NIDDK executive officer, was honored with the National Kidney Foundation's George M. O'Brien Award in recognition of his longtime support of coordinating foundation programs with NIDDK ... **Dr. Donald A.B. Lindberg,** NLM director, received the Meritorious Presidential Rank Award "for instituting at the National Library of Medicine sophisticated and successful information programs and services responsive to the needs of the nation's health professionals in dealing with biotechnology, AIDS, and other contemporary issues in medicine" ... **Julia Lobotsky,** head of the reproductive biology section of the Reproductive Sciences Branch, Center for Population Research, NICHD, received two awards from organizations concerned with the reproductive sciences. She was given a Lifetime Achievement Award at the Endocrine Society's 72nd annual meeting in Atlanta in recognition of "her tireless efforts in support of biomedical research, relentless pursuit of excellence and unending empathy for investigators." She was also presented with the Distinguished Service Award from the Society for the Study of Reproduction at its 23rd annual meeting in Knoxville for her "invaluable contribution to the membership of the SSR and the fields of reproductive biology and endocrinology as a whole" ... **John D. Mahoney,** director of NIH's Office of Administration, received the Meritorious Presidential Rank Award "for outstanding leadership and management skill

(See NIH Notes p. 27)

NIH Notes *(continued from p. 26)*

in restructuring NIH station support procurement operations, achieving significant cost savings, and developing unprecedented levels of regulatory compliance while maintaining system responsiveness to research needs" ... **Dr. Malcolm A. Martin,** chief of NIAID's Laboratory of Molecular Microbiology, received a Meritorious Presidential Rank Award "for exceptional leadership and sustained accomplishments in research on the retrovirus that causes AIDS and for important scientific studies relating to RNA and DNA viral genome structure of biological functions which have advanced the use of recombinant DNA technology" ... **Carolyn G. McHale,** chief of the NIAMS Scientific Information and Data Systems Branch, was the recipient of the 1990 Harriet E. Worrell Award from Drexel University for "a distinguished career in medical research and information systems." The award is given annually to outstanding alumni of the university ... **Dr. Ralph F. Naunton,** director of the Division of Communicative and Neurosensory Disorders, NIDCD, was the Carhart Memorial speaker at the 1990 annual meeting of the American Auditory Society held in Seattle. Before coming to NIH he was chairman of the department of otolaryngology at the University of Chicago ... **Dr. William F. Paul,** chief of the Laboratory of Immunology, NIAID, was one of the 24 internationally renowned biomedical scientists who spoke recently at the Irvington Institute for Medical Research's 75th anniversary symposium "Immunology in the 21st Century" in New York City. His theme was "Lymphokines: Molecular Mediators of the Immune Response" ... **Dr. Philip A. Pizzo,** chief of NCI's Pediatrics Branch, was honored in the January issue of *Washingtonian* magazine as a "Washingtonian of the Year." He shared the honor with three congressional wives, Carmala Walgren, Debbie Dingell, and D. Chris Downey, who were the officers of the Friends of the Children's Inn, a nonprofit organization that helped raise funds to build the inn ... **Dr. Eric Ravussin,** an NIDDK scientist at the Phoenix Epidemiology and Clinical Research Branch in Arizona, received the Andre Mayer Award for outstanding research in obesity at the 6th International Congress on Obesity in Kobe, Japan. He came to Phoenix from Switzerland in 1984 to set up a respiratory chamber, the first in the United States, to measure daily metabolic rates in relationship to body weight changes ... **Dr. Matilda W. Riley,** associate director of NIA's Behavioral and Social Research Program, received the Meritorious Presidential Rank Award "for outstanding leadership and significant accomplishment in the establishment of a national and international extramural program of social and behavioral research at the National Institute on Aging" ... **Dr. Gustavo C. Roman,** chief of NINDS' Neuroepidemiology Branch, has been named co-editor of *The Journal of Tropical and Geographical Neurology*, a quarterly peer-reviewed journal newly created by the research group on tropical neurology of the World Federation of Neurology ... **Dr. Marcel Salive,** an epidemiologist in NIA's Epidemiology, Demography, and Biometry Program, has received the Jay S. Drotman Award from the American Public Health Association ... **Dr. James B. Snow, Jr.,** NIDCD director, gave keynote addresses at the American Indian Research Symposium in Montana and the centennial address at the Alexander Graham Bell Association for the Deaf ... **Dr. Novera Herbert Spector,** NINDS health scientist administrator, recently received a medal commemorating the 100th anniversary of the Polish Physiology Society in recognition of his contribution to basic research in physiology, especially on interactions among the nervous, endocrine and immune systems ... **Dr. Allen Spiegel,** NIDDK acting scientific director, recently gave the 1990 Jacobaeus Lecture in Oslo, Norway. He spoke on the structure and function of G proteins, which act as intermediaries in cell signaling.

APPOINTMENTS AND PERSONNEL CHANGES

Dr. James Anderson, former head of the department of molecular genetics at Crop Genetics International in Hanover, Md., has been appointed a program administrator in the Genetics Program, NIGMS. He will handle grants in the areas of physiology of gene control and RNA processing ... **Dr. David Benton** has joined the National Center for Human Genome Research as assistant to the director for scientific data management to oversee the "informatics" program to develop computer technologies able to meet the needs of the genome project. He comes to NCHGR from the West Coast technology company IntelliGenetics, Inc., where he managed the DNA sequence database GenBank ... **Dr. Carlos E. Caban,** program director for cancer control research in the Division of Cancer Prevention and Control, NCI, has been named extramural programs policy officer in the Office of Extramural Research, Office of the Director, NIH. He is responsible for reviewing, evaluating and advising on current and proposed regulations, policies and procedures used in management of NIH-ICD extramural research and development programs, with emphasis on use of cooperative agreement and contract mechanisms and peer review policies and procedures ... **Dr. Eliezar Dawidowicz,** an associate professor of physiology at Tufts Medical School, has been appointed a program administrator in the Cellular and Molecular Basis of Disease Program, NIGMS. He will handle grants in the areas of membrane and lipid metabolism and membrane transport ... **Carlos M. Delgado** has joined the Division of Equal Opportunity as chief of the Equal Opportunity Branch. In his new position, he works to foster and promote equal opportunity principles throughout NIH ... **Marian Emr,** most recently NIA's deputy information officer, has been appointed information officer for the National Institute of Neurological Disorders and Stroke. She comes to NINDS with 14 years of experience in medical writing, media relations and public information at NIMH and NIH ... **Raymond Fleming** has been named information officer for DCRT. He comes from NINDS, where he was deputy information officer ... **Dr. Steven J. Hausman,** deputy director of the NIAMS extramural program, has been appointed NIAMS' first deputy director ... **Dr. Richard Havlik** has been named associate director of NIA's Epidemiology, Demography, and Biometry Program. He will direct epidemiology studies that look at aging processes and identify differences between "usual aging" and the onset of diseases ... **Colleen Henrichsen,** chief of the DCRT Information Office, has been appointed chief of the Clinical Center Communications office ... **Dr. Caroline Holloway,** head of the biological structure section of the Biomedical Research Technology Program, NCRR, and executive secretary to the biomedical research technology review committee, has been named director of the Office of Science Policy, NCRR. This newly organized office includes both extramural and intramural responsibility for program planning, analysis and evaluation; legislation, and science policy within the office of the director of NCRR ... **Dr. Joye F. Jones,** chief of the genetics of growth and differentiation section of NIGMS Genetics Program since 1989, has been named deputy associate director for

(continued on p. 28)

NIH Notes *(continued from p. 27)*

program activities, NIGMS ... **Dr. Lewis L. Judd,** director of NIMH since 1988, has recently returned to University of California, San Diego School of Medicine as chairman of the department of psychiatry. During Judd's tenure at NIMH, national research initiatives were implemented in three key areas: schizophrenia, neuroscience, and child and adolescent mental disorders. A fourth project, a research plan to improve the care of individuals with persistent and severe mental disorders, is in the final stages of development. Dr. Alan I. Leshner, NIMH deputy director, will serve as acting director of the institute while a search for a new director is conducted ... **Dr. Dennis E. Leszczynski,** a senior research scientist and executive director of the Harlan E. Moore Heart Research Foundation, a private not-for-profit corporation affiliated with the University of Illinois, has joined the Division of Research Grants as an executive secretary in the Referral and Review Branch ... **Dr. G. Iris Obrams** has been appointed chief of the Extramural Programs Branch in the Epidemiology and Biostatistics Program, Division of Cancer Etiology, NCI ... **Christine Wisdom** has been named NIGMS deputy executive officer. She has worked at NIH for the past 14 years. Most recently, she was on a 20-month detail from the Division of Legislative Analysis to the Labor/HHS/Education subcommittee of the House of Representatives committee on appropriations ... **Dr. Rosemary Yancik,** a medical sociologist with a longstanding interest in aging, has joined the National Institute on Aging as assistant director for liaison and applied research on aging. Her research interests have focused on the areas of cancer and aging. She was in the Office of Extramural Research, OD, before joining NIA. She also held several positions at NCI, including assistant director for centers and community oncology, Division of Cancer Prevention and Control. She joined NIH in 1978. In her new job she will help develop collaborative programs to investigate how cancer and other diseases affect the older population.

RETIREMENTS

Regina Dowling retired from the department of transfusion medicine at the Clinical Center. She had worked at NIH for 27 years. She first came to NIH in 1963 as a part-time nurse and finished her career at the CC as a patient apheresis supervisor. She plans to pursue other interests such as volunteer work in her church and community and to travel with her husband ... **Dr. Michael M. Frank,** chief of NIAID's Laboratory of Clinical Investigation, retired Dec. 1 to become professor and chairman, department of pediatrics at Duke University Medical Center. His research interests, broadly described, involved the relationship between immune mechanisms in host defense and immune damage in the development of disease. His pursuits in this area led him to examine how these processes interrelate with immune complexes and, ultimately, with complement activation. Also notable in Frank's NIAID career was his ability to recognize talent among those who applied for positions in his lab and, in addition, to nurture the development of his staff members. His former staff fellows now head major academic medical units in infectious diseases, hematology, allergy/immunology, rheumatology, dermatology and pulmonary medicine ... **Dr. Preston A. Littleton, Jr.,** NIDR deputy director and PHS deputy chief dental officer, retired on Sept. 17 to become executive director of the American Association of Dental Schools ... **Dr. Paul O'Brien,** acting director, NEI Intramural Research Programs and chief, section of cell biology, Laboratory of Retinal Cell and Molecular Biology, retired Sept. 1, his 30th anniversary with NIH, and his 20th with NEI. He plans to keep in touch with the scientific community through his new job at a private company that helps researchers prepare grant applications ... **Ira "Robbie" Robinson,** supply clerk in the Management Services Branch, NIAID, has retired after 34 years at NIH. In 1957 he began his career at NIH in the Clinical Center housekeeping unit. Five years later he transferred to NIAID. He is looking forward to spending more time with his family and also plans to do some fishing... **Dr. Jesse Roth,** scientific director for NIDDK's Division of Intramural Research since 1981, retired in December 1990. His 27 years at NIH have been marked by seminal work on hormones and their receptors. He has had an important role in helping young investigators around the world, expanding endocrine research to centers in Europe, Israel and Japan as well as in the United States. He has moved to the Johns Hopkins School of Medicine, where he is professor of medicine and gerontology.

DEATHS

Geraldine "Gerri" Brammer, died Oct. 17. She was an EKG technician in CC since 1978 and worked at NIH for the past 17 years ... **Clara Chesney Crouch,** 101, died Jan. 16 in Silver Spring. She worked at NIH from 1946 until 1957 as a clerk ... **Dr. Joseph W. Cullen,** 53, former deputy director of the Division of Cancer Prevention and Control, NCI, died of a brain tumor Nov. 24 at St. Luke's Hospital in San Francisco. He had left NIH in July 1989 to become director of the AMC Cancer Research Center in Denver. During his NCI career, he directed the institute's program to eliminate cigarette smoking, which gave major impetus to federal anti-smoking efforts ... **Levi Dargan,** a computer program analyst in the Division of Computer Research and Technology, died Dec. 29. He had served the division's Computer Center Branch for more than 21 years. He began his career at DCRT as a computer operator in 1969. After being promoted to computer programmer in the program support section, he worked closely with NIH accounting systems to set up computer programs that would run throughout the night. He was active in his community and his church ... **Roberta Pierce Davis,** 69, an executive secretary for 20 years at NIH, died of cancer Jan. 24 at a hospital in Hanover, Pa. In 1981 she retired from the National Institute of Arthritis and Musculoskeletal and Skin Diseases ... **Dr. Kenneth Fitch,** a health scientist administrator in the Division of Research Grants, passed away on Dec. 4 of cancer. He was executive secretary in the special review section of DRG's Referral and Review Branch. His NIH career began in 1981 where he became an expert consultant with NCI. In 1987 he became an employee of NIAID, later transferring to NHLBI, and in 1989, he joined DRG ... **James U. Genies,** 78, a retired employee at NIH, died of heart disease Jan. 14 at his home ... **Frank G. Hickerson,** 65, a retired NIH architect, died Dec. 1 at his home after a heart attack. He worked at NIH for 25 years before retiring ... **Mary Clifford "Maureen" Hornish,** 60, who had worked as a psychiatric nurse at the National Institute of Mental Health, died of cancer Nov. 14 in Bedford, Mass. ... **Dr. David Lackman,** 79, a research scientist in serology and virology at Rocky Mountain Laboratory, NIAID, in Hamilton, Mont., died Nov. 3 in Helena after a long illness with cancer. He worked at the RML from 1941 un-

til his retirement in 1966. Since 1977 he had been a volunteer legislative lobbyist for the Montana Health Association ... **Dr. Patricia McGovern,** 54, a researcher who specialized in kidney and liver ailments, died of kidney and heart ailments Jan. 16 at Suburban Hospital. She was a medical researcher who worked at home; she also worked for physicians in private practice and at NIH ... **Charles Bogart Myers,** 70, a retired management analyst with NIH, died of congestive heart failure Nov. 18 at his home. He came to NIH in 1961 to work in the Office of the Director and later as management analysis officer at NIAID. He retired in 1978 ... **Dr. Louis J. Olivier,** known for his early schistosomiasis research at NIAID, died in Chapel Hill, N.C., on Nov. 16. In 1946, after completing service in the Army's malaria survey unit, he joined the PHS, where he headed the host-parasite relations section of the lab that was later to evolve into NIAID's Laboratory of Parasitic Diseases. Following his retirement in 1966, he continued in the parasitology field working for 5 years as regional advisor on parasitic diseases for the Pan American Health Organization. He then spent 2 years in Geneva as a consultant to the World Health Organization ... **Robert J. Schultheisz,** a systems analyst in the Office of Computer and Communications Systems, NLM, died Nov. 28 following surgery for cancer. He had worked at NLM since 1970, and for the federal government for more than 30 years. At NLM, he was initially employed in Specialized Information Services developing databases in toxicology. Most recently he had been part of the Development Branch of OCCS working on the MEDLARS III and the TESS (Technical Services System) projects ... **Dr. Irving "Ozzie" Simos,** 68, a psychologist who retired from the Division of Research Grants in 1987, died Dec. 9 of amyotrophic lateral sclerosis. He had a distinguished and well-respected career at NIH that spanned 30 years. He held positions that included executive secretary of the small grants section at NIMH, and deputy chief of the Referral and Review Branch, DRG. After his retirement from NIH, he pursued his hobby of violin playing and volunteered as a counselor ... **Jane Stafford,** 91, a science writer and retired assistant director of information at NIH, died of cardiac arrest Jan. 11 at Menno-Haven nursing home in Chambersburg, Pa. She came to Washington in 1928 as a science and medical writer and joined the staff at NIH in 1956. She retired in 1971.

Rep. Silvio O. Conte, (R-Mass.), 69, died Feb. 8 at the Clinical Center of extensive bleeding in the brain stemming from the progression of prostate cancer, for which he underwent surgery in 1987. Conte was the senior Republican on the House appropriations committee and was beginning his 17th term in Congress. Throughout his long legislative career he was a strong, effective supporter of medical research. The new Child Health and Neurosciences Facility, Bldg. 49, for which he worked for more than a decade to fund, has been named in his honor. At the groundbreaking ceremony on Oct. 4, 1988, (pictured above) he called it "the proudest achievement in all my years in office."

Right Conte hugs Clinical Center patient Brianne Schwantes of Milwaukee at the groundbreaking ceremony for Bldg. 49.

Recent Books of Interest To NIHAA Members

Dr. Victoria A. Harden, *Rocky Mountain Spotted Fever: History of a Twentieth-Century Disease*. Baltimore: Johns Hopkins University Press, 1990.

Prepared for the National Institute of Allergy and Infectious Diseases, this book traces the history of research on Rocky Mountain spotted fever (RMSF) from the late 19th century, when it was first identified as a distinct disease, to the present. Research on RMSF represents one of NIH's oldest continuous investigations and one of the earliest federal-state cooperative research efforts. Harden is the Director, NIH Historical Office and DeWitt Stetten, Jr. Museum of Medical Research and is the author of *Inventing the NIH: Federal Biomedical Research Policy, 1887-1937*, also published by Johns Hopkins.

Stephen P. Strickland, *The Story of the NIH Grants Programs*. Lanham, Md., and London: University Press of America, 1989.

Well known as the author of *Politics, Science, and Dread Disease*, Stephen Strickland has surveyed in this book the emergence of federal support for biomedical research after World War II as embodied in the grants program of the NIH. The book is based on oral histories with participants who shaped the program and conveys well the flavor of this period of NIH expansion.

NIH Retrospectives

N.I.H. record

FEDERAL SECURITY AGENCY — PUBLIC HEALTH SERVICE, NATIONAL INSTITUTES OF HEALTH

SPRING 1951

The NIH Hamsters presented a second hit show titled "Carmen Cold" ... NIH scientists made substantial contributions to a recently issued booklet *Health Services and Special Weapons Defense*, prepared by the Health Resources Office, NSRB. The 260-page booklet explains the effects of weapons ranging from atom bombs to nerve gases and outlines the functions, responsibilities and organization of civil defense health services ... Dr. Jack Masur, Chief of the Research Facilities Planning Branch at NIH, has been appointed Chief of the Bureau Services, PHS, succeeding Dr. R.C. Williams who retired ... Investigations by NIH scientists have linked the A group of Coxsackie viruses with herpangina, a mild illness of widespread occurrence, especially among children, which has caused a fear of polio because of similar symptoms. Prior to the NIH studies, however, physicians had found its symptoms puzzling and mistook herpangina for other throat conditions.

the Record

SPRING 1961

A Joint Committee on Cancer Information has been established by the National Cancer Institute and the Cancer Control Branch, Bureau of State Services, to coordinate the planning, production, and distribution of public and professional information material relating to cancer research and control ... Dr. Luther L. Terry, 49, Assistant Director of the National Heart Institute, has been appointed Surgeon General of the Public Health Service, by President Kennedy ... The National Institute of Arthritis and Metabolic Diseases observed its tenth anniversary in a day-long program of activities including a special "Report to the Nation" on its 10 years of research.

the NIH Record

SPRING 1971

A cluster of our new buildings was dedicated on March 1 at the National Institute of Environmental Health Sciences Center, Research Triangle Park, North Carolina. Dr. David P. Rall, associate scientific director of NCI, supervising experimental therapeutic programs, has been named the new director succeeding Dr. Paul Kotin ... President Nixon creates a new group to plan and direct expanded cancer research effort ... HEW Secretary Elliot L. Richardson visited NIH in mid-March and has a question and answer session with employees ... A dedication ceremony was held at the Fogarty International Center for the unveiling of a bronze sculpture of the late Congressman John E. Fogarty of Rhode Island.

The NIH Record

SPRING 1981

Several hundred Federal arrest warrants have been recently issued for employees who have failed to pay the fines on their traffic tickets ... President Carter's fiscal year 1982 request for NIH is $3,848,689,000, a net increase of $255 million above the 1981 level being recommended by the Administration ... "Graduates" of Dr. Christian B. Anfinsen's school—his intramural laboratories—gathered in Masur Auditorium to participate in an International Symposium on the Contributions of Chemical Biology to the Biomedical Sciences ... An exhibit and bust honoring Dr. Charles R. Drew, known as the "Father of the American Blood Bank," was unveiled at NIH, making it the first permanent exhibit honoring a black physician on the NIH campus.

This photograph is from the prints and photographs collection at the National Library of Medicine. The curator, Lucinda Keister, would like to know if anyone recognizes the participants and event. Please send details to *Update*.

Attention

NIHAA wants to hear from its members. Please type or print your note for a future issue and mail it to:

Harriet R. Greenwald, Editor
NIHAA Update
9101 Old Georgetown Rd.
Bethesda, MD 20814

Name

Home address **Home phone**

News. Include dates/position at NIH and photo if possible.

Suggestions for newsletter

What is Happening with the NIH Alumni Association?

In March, the board of directors elected officers for 1991-92. They are president, Dr. Joe R. Held; vice president, Dr. John F. Sherman; and secretary-treasurer, Calvin B. Baldwin Jr.

The association has two events scheduled for May. The first is a reception at the AAP/ASCI/AFCR meeting on Saturday, May 4, from 5 to 7 p.m. in the Madrona Seattle Sheraton Hotel and Towers. Please attend if you are at the meeting. The second event is a reception to honor the visiting scientists at NIH from Italy, which will be on Tuesday, May 21, at 7 p.m. It will be sponsored by the Washington area chapter of NIHAA. Invitations will be sent in April.

International and local domestic chapters are being established. Dr. James A. Pittman Jr., Dean, University of Alabama School of Medicine, is heading our first local chapter. On Apr. 5, Dr. J. Edward Rall, NIH deputy director for intramural research, will be the guest speaker at the first meeting. We will have pictures and coverage in our next *Update*. Letters have been sent to more than 20 foreign countries asking former NIH'ers about establishing chapters. The response so far has been enthusiastic. We will have more specifics in the next newsletter.

As part of Research Festival '91, NHLBI will sponsor an NIH symposium Monday, Sept. 23, to honor a distinguished alumnus. More information and a description of the program and other related activities will appear in the summer newsletter.

Reaction to *Update* continues to be complimentary, but we would like to hear more from our members. We invite you to send the above clip-out form with your news. Please include comments and suggestions both for the association and for the newsletter.