

The NIH Record

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National
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of
Health

Dr. Bruce Chabner Named NCI Division Director

Dr. Bruce A. Chabner has been appointed director of the Division of Cancer Treatment, National Cancer Institute. He has been acting director of the division since 1981.

The Division of Cancer Treatment plans, directs and coordinates integrated research nationwide to improve treatment of cancer patients. Among DCT's major programs are research efforts in surgery, radiotherapy, chemotherapy, patient nutrition, and biological response modifiers, substances that may be used to boost the body's natural defenses against cancer.

Dr. Chabner began his career in the pharmacology of anticancer drugs (their mechanisms of action) as a clinical associate at NCI from 1967 to 1969. He then became a research associate at Yale University School of Medicine in 1970.

The following year he joined NCI as senior staff fellow and senior investigator in the Laboratory of Chemical Pharmacology and Solid Tumor Service. He became senior investigator in that laboratory from 1972 to 1975, and head of its biochemical pharmacology section from 1973 to 1975. From 1972 to 1975 he also served as senior investigator



Dr. Chabner has a long research background centering on the biochemistry and clinical pharmacology of antimetabolites, a class of anticancer drugs that interferes with the use of normal nutrients by cancer cells, thus preventing their continued growth.

in the Medicine Branch of DCT.

His career at NCI has spanned basic research on the biochemistry and pharmacology of anticancer drugs, their clinical application, and the direct clinical management of cancer patients.

(See Dr. CHABNER, Page 5)

Two New Director Appointments Announced By NIH Director Dr. James B. Wyngaarden Dr. Harald Løe

Dr. Harald Løe has been appointed Director of the National Institute of Dental Research pending approval of the Office of Personnel Management.

Dr. Løe, who is currently dean of the University of Connecticut School of Dental Medicine, will assume his new position Jan. 1

NIDR, established as an NIH Institute in 1948, conducts and supports research into the causes, prevention, diagnosis and treatment of oral and dental diseases and conditions.



Dr. Løe, a native of Norway, received both the doctor of dental surgery and doctor of odontology degrees from the University of Oslo. Universities in four countries—Sweden, Denmark, Greece, and Belgium—have awarded Dr. Loe honorary degrees.

Widely recognized for his contribution in the field of periodontology, Dr. Løe is also known for his service in dental education. In his distinguished professional career, he has been in clinical practice, and held teaching positions in dental colleges at Oslo University, Hebrew University (Israel), the Royal Dental College (Aarhus, Denmark), the University of Michigan, and the University of Connecticut.

He was elected dean of the Royal Dental College of Aarhus, Denmark, and also served as director of the University of Michigan's Dental Research Institute.

Dr. Løe has published extensively in his research field and is the founding editor of the *Journal of Periodontal Research*. He has lectured throughout the world and is past president of the International Association for Dental Research. □

Dr. Betty H. Pickett

Dr. Betty H. Pickett has been appointed Director of the Division of Research Resources. Dr. Pickett, who is currently deputy director of the National Institute of Child Health and Human Development, will assume her new position Oct. 1.

The DRR is responsible for creating, developing and making available a broad base of centers, resources, and institutional support required by the biomedical research activities of NIH and other research components of the Public Health Service.



Dr. Pickett has been deputy director of NICHHD since 1979. She was Acting Director of the Institute from July 1981 to July 1982. Prior to joining the NICHHD, Dr. Pickett served for 2 years as associate director for extramural and collaborative research of the National Institute on Aging.

Her previous experience includes a number of senior positions in the National Institute of Mental Health and service as executive secretary of two study sections in the NIH Division of Research Grants following her appointment to the PHS in 1958.

A native of Rhode Island, Dr. Pickett received her academic training at Brown University earning an A.B. degree in 1945 and a Ph.D. in psychology in 1949.

She has received numerous honors and awards, including the HEW Distinguished Service Award in 1975, the Harold M. Hildreth Award from the American Psychological Association in 1979 for distinguished contributions to psychology in the public service, and the Senior Executive Service Outstanding Performance Award in 1981. □

The NIH Record

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Training Tips

The following courses, sponsored by the Division of Personnel Management, are given in Bldg. 31 unless otherwise indicated.

Communication Skills	Course Starts	Deadline
Freedom of Information	11/10	10/25
Workshop for Grants Staff	11/17	
Office Skills		
Proofreading	10/13	9/29
Effective English Workshop	10/18	9/29
Supervisory and Management		
Planning for Prevention and Results	10/20	10/8
Behavioral Strategies for Supervisors and Managers	10/27	10/15

* These courses are offered in Westwood Bldg.

To learn more about these and other courses in office and communication skills, contact the Training Assistance Branch, DPM, 496-2146.

For further information on supervisory and management courses, contact the Executive and Management Development Branch, DPM, 496-6371.

Karate Classes Now Forming

NIH Karate Club's beginner, intermediate, and advanced Tae Kwon Do (Karate) classes are now forming. All classes begin Monday, Oct. 18, at the Stone Ridge School gymnasium, corner of Cedar Lane and Wisconsin Ave.

Beginners class is from 6-7 p.m.; intermediates 7-7:45 p.m.; advanced intermediates, 7:45-8:30 p.m.; and advanced 8:30-9:30 p.m. The fee for beginners is \$35, and \$15 for intermediates and advanced. To register, contact Dr. W. French Anderson, 496-5844. □

Reservation Toured by HHS Officials



A number of HHS regional directors and intergovernmental and congressional affairs and press officers recently visited the campus for the express purpose of becoming more familiar with the facilities and operations of NIH.

The tour of the campus was conducted by Huly Bray, NIH Special Projects Officer and Assistant to the Director for Protocol.

Storm Whaley, NIH Associate Director for Communications, welcomed the group on behalf of the NIH Director. Dr. Jay Shapiro, Acting Clinical Center Director, welcomed

them to the Warren Grant Magnuson Clinical Center.

While at the CC, the visitors briefly toured the ACRF with stops in the Nuclear Medicine and Clinical Pathology departments, the 13th floor clinic, laboratory and material handling areas and the Visitors Center.

A regional director is the personal representative of the HHS Secretary responsible for carrying out the Secretary's departmental policies in each of the 10 HHS regions throughout the United States. □

Science Writers' Seminar On Oncogenes Is Oct. 14

The NIH Science Writers' Seminar on Oncogenes—the genes in tumors which when transferred to normal cells can make them cancerous—will be held on Oct. 14, from 1:30 to 4 p.m., in the ACRF Amphitheater.

Dr. George Khoury, chief, Laboratory of Molecular Virology, NCI, will open the program with a discussion on the control of the level of gene expression.

Oncogenic transformation by viral and cellular genes will be the subject of a talk by Dr. George Vande Woude, chief, Laboratory of Molecular Oncology, NCI.

The moderator of the seminar, Dr. Douglas R. Lowy, deputy chief of NCI's Dermatology Branch, will describe the progress that has been made in research on a family of closely related human and animal oncogenes.

The presentation by Dr. Mariano Barbacid, a visiting scientist in NCI's Laboratory of Cellular and Molecular Biology, will cover studies of oncogenes in human tumors.

Dr. Robert C. Gallo, chief, Laboratory of Tumor Cell Biology, NCI, will discuss human leukemia virus infection and gene activation.

Science Writers' Seminars, sponsored by the intramural scientists of NIH and the Division of Public Information, OD, are designed to provide members of the press with background information on the various areas of research conducted here at NIH.

For additional information, call Bobbi Bennett, 496-1766. □

'Operation Backfill' in Motion

When the construction of the Ambulatory Care Research Facility building commenced in the spring of 1977, it was necessary to relocate several BID organizational components to Bldg. 31 in order to vacate areas of Bldg. 10 that would become an integral part of the new structure.

With the completion of the ACRF and the earlier phases of the Bldg. 10 modernization program, these components are now in the process of returning to Bldg. 10. The space being vacated in Bldg. 31 has recently been reassigned by NIH Director Dr. James B. Wyngaarden and will result in an extensive backfill operation.

Included in this reassignment are provisions for the NIH Federal Credit Union to return to the NIH reservation from their present accommodations on Old Georgetown Road.

Plans to facilitate "Operation Backfill" are presently being developed by Space Management, NIH. It is expected that the project will extend over a period of from 6 to 10 months. □

Attention: Disabled Veterans

A recruitment plan is being organized for disabled American veterans to form a national organization to pursue a matter of interest to them as well as their dependents and survivors. NIH veterans can contact Bob McDevitt at 496-1956 for further details. □

Health Resources, Services Administration Consolidated To Form New PHS Agency

Dr. Edward N. Brandt, Jr., Assistant Secretary for Health, recently announced the formation of a new PHS agency, the Health Resources and Services Administration, effective Sept. 1.

"The new agency will provide leadership and direction for programs to provide direct health services for certain population groups, and to develop the resources necessary for the health care system of the future," Dr. Brandt said.

Dr. Robert Graham, who has been serving as acting administrator of the Health Resources Administration, will be administrator of the new agency. John H. Kelso will be deputy administrator. He is currently acting administrator of the Health Services Administration.

The Health Resources and Services Administration consolidates the following PHS programs into four bureaus:

Indian Health Service. Transfers from HSA with no change in organization and functions. The IHS will continue to ensure a comprehensive health services delivery system for American Indians and Alaska Natives. Dr. Everett R. Rhodes will continue as director.

Bureau of Health Maintenance Organizations and Resource Development. Consolidates the Office of Health Maintenance Organizations from the Office of the Assistant Secretary for Health, and HRA's Bureau of Health Planning and Bureau of Health Facilities. Dr. Daniel F. Whiteside has been appointed director.

Bureau of Health Professions. Will provide leadership in coordinating, evaluating and supporting the development and utilization of the nation's health personnel. Dr. Thomas Hatch will continue as director.

Bureau of Health Care Delivery and Assistance. Combines programs from HSA's Bureau of Community Health Services, Bureau of Medical Services, and the National Health Service Corps (including scholarships), now administered by the Bureau of Health Personnel Development and Service. Dr. John Marshall will serve as acting director.

The bureau will act as a national focus for efforts ensuring the availability and delivery of health care services in medically underserved areas and to special services populations.

Headquarters for the new agency will be Rm. 14-05 of the Parklawn Bldg., 5600 Fishers Lane, Rockville, Md. 20857; (301) 443-2216. □

Music for Your Ears

Scandinavia Today, featuring new music from the Northern countries, is the theme of the Contemporary Music Forum's free noon-time lecture and opening concert on Monday, Oct. 4, in the Masur Auditorium.

Tickets to the concert will be available at the door or through R&W, sponsors of the new series of six monthly evening concerts of 20th century music. □

Career Day Program To Be Held Oct. 14

Career Day, sponsored by the Women's Advisory Committee and the NIH Federal Women's Program, will be held Thursday, Oct. 14, in Wilson Hall, Bldg. 1, from 10 a.m. to 2 p.m.

Information on career change and development, career paths, continuing education, and various personnel topics will be provided at information exchange resource areas.

Employees will also have an opportunity to discuss with representatives from various occupations the duties and responsibilities involved in those occupations.

Experts will be available to answer questions about many topics including career paths—what kinds of jobs are included and work required; career change and development—what opportunities and programs are available at NIH, and what the eligibility requirements are; personnel information—how the new employee performance management system works, and what rights employees have under this system.

Career change and advancement will con-



National Aquarium Visit Planned

R&W plans a visit to the National Aquarium and Harbor Place in Baltimore on Saturday, Nov. 6. The aquarium contains over 8,000 types of water life.

Buses will leave Bldg. 31C at 10 a.m., and will depart from Baltimore at 4 p.m. The cost, \$10.50 for adults and \$8.50 for children under 12, includes transportation and admission.

Interested persons may sign up at the R&W Activities Desk, Bldg. 31, Rm. 1A18. □

Watch Them Toss Baskets

The NIH R&W basketball league will open the season on Tuesday, Oct. 5, in the Clinical Center's gymnasium. Games will be played every Tuesday and Thursday evening, starting at 5:30 and 6:30 p.m., until the championship in March. Eight teams will be trying to upset last year's champs, the "Blades," who had a record of 13 and one. All NIH employees are invited to watch the games. □

A lie has no legs and cannot stand, but it has wings and can fly far and wide.

—Unknown □



tinue to be highly competitive. Career Day is a forum for all NIH employees to obtain information about career options and issues affecting those options.

Linda Bremmerman, vice chairperson of the WAC and delegate from the National Cancer Institute, is chairing the Career Day committee.

Claire McCullough, the delegate from the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, chairs the WAC; and Barbara Iba is the acting Federal Women's Program manager in the Division of Equal Opportunity.

Dr. Ursula Lohmann, employee development specialist, Training and Development, Division of Personnel Management, is providing career development expertise and technical guidance.

Sign language interpretation will be available. Assistance with physical access will also be available on request. For more information and assistance, call the NIH FWP office, 496-2112. □

A Message From Mrs. Thompson

The following is a message of appreciation from Elizabeth Kay Thompson, wife of Lloyd Thompson who died Aug. 30 of injuries received in an explosion.

The family of Lloyd Thompson wishes to express a sincere appreciation for the deep concern shown by friends and coworkers in the matter of Lloyd's mishap and demise.

"We extend special thanks to friends who generously donated blood and offered contributions to the Washington Hospital Burn Unit. The cash donations received from the Clinical Center section, the elevator section and the power plant section of the Maintenance Engineering Branch, along with the other donations, were given to the burn unit.

We would also like to acknowledge the members of the NIH Fire Department and the Paramedic Team and the gallant efforts taken to keep Lloyd alive at the accident site and in transport to the hospital.

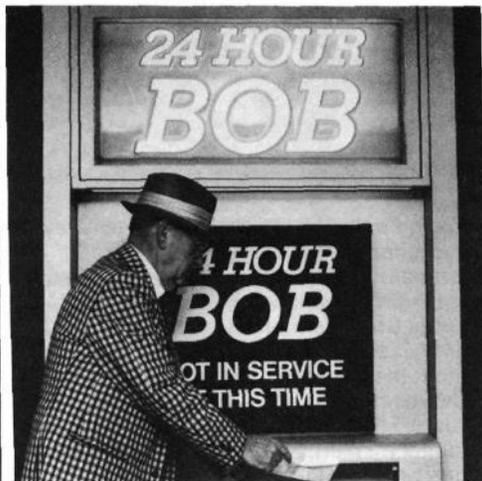
Although it is impossible for us to thank each and everyone personally, there is one man whose kindness touched us all—Mr. Andrew W. Klassett, his foreman. We thank you all from the bottom of our hearts."

The Thompson Family

Automatic Teller Machine To Open in Bldg. 10

"24-Hour BOB" is the name of the new automatic teller machine recently installed in Bldg. 10 by the Bank of Bethesda. The ATM will be operating from the first teller window on the left, adjacent to the Automatic Post Office, on the B1 level.

The ATM is expected to be operating by early October, with 24-hour-service offered for various banking transactions. Nine other



24-hour BOB machines are being installed at other bank locations in Montgomery County.

The Bank of Bethesda has joined the "MOST system," a group of financial institutions in Maryland, Washington, D.C., and Virginia, who will share use of their ATM's. Any member of the NIH staff having an account with one of these financial institutions can make cash withdrawals and balance inquiries at NIH and any other ATM location of the Bank of Bethesda.

Currently, the MOST system has more than 70 financial institutions as members. A complete list of the participants in the network can be obtained from the Bank of Bethesda.

In order to improve communication and ensure optimum service for NIH employees, Calvin B. Baldwin, Jr., NIH Associate Director for Administration, and Dr. Edwin D. Becker, NIH Associate Director for Research Services, have been meeting with Bank of Bethesda officials.

Suggestions for any improvements in services are welcomed by the bank's branch manager, Joyce Grimm. In addition, comments or suggestions may be sent to Mr. Baldwin or Dr. Becker through the space management staff of the Office of Research Services, 496-3172. □

CLEP Exam Offered

NIH employees can participate in the college-level examination program (CLEP) when it is conducted on Thursday, Oct. 28. CLEP is a nationally recognized testing program where individuals can receive college credit for knowledge they have obtained outside of school. Deadline for test registration is Oct. 7.

Information about CLEP can be obtained from Carol Daniels, Career Education Center, Bldg. 31, Rm. 4B03, or by calling 496-5025. □

Multicenter Study Will Evaluate Plasmapheresis for Lupus Patients

A new nationwide multicenter study to determine the value of using plasmapheresis, a blood-separating process, to treat patients with severe lupus nephritis is being supported by the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases.

Lupus (systemic lupus erythematosus) is a serious chronic inflammatory disease of the connective tissue, estimated to affect approximately 500,000 people in the United States, primarily young women. Lupus nephritis refers to the form of the disease that includes inflammation of the kidneys.

Plasmapheresis is a technique of removing plasma from a patient's blood, and replacing it with plasma or a plasma substitute that does not contain the destructive antibodies found in lupus.

According to Dr. Nancy B. Cummings, NIADDK's associate director for Kidney, Urologic, and Hematologic Diseases, the purpose of this study is to determine whether or not plasmapheresis has a beneficial effect on patients with lupus nephritis, and to provide a mechanism for developing a standardized definition of lupus nephritis, and guidelines for managing the renal involvement in the disease.

After a pilot study, NIADDK grantee Dr. Edmund J. Lewis, director of the section of nephrology, and his associates at Rush-Presbyterian-St. Luke's Medical Center in Chicago, reported that plasmapheresis removed a large amount of damaging "immune complexes" (abnormal components) from the blood of patients.

Scientists think that kidney failure and other manifestations of lupus may be directly related to injury caused by the presence of these abnormal components in

patients' blood plasma.

Approximately 10 treatments at about \$1,000 each, are used for each patient's course of therapy. Reports of the success of plasmapheresis have prompted more widespread use of this therapy combined with drug treatment, even though it has not yet been proved scientifically effective.

In April 1981, NIADDK awarded a grant to Dr. Lewis to conduct a controlled prospective study on the effects of plasmapheresis on the short- and long-term courses of patients with severe forms of lupus nephritis. As principal investigator for the study, Dr. Lewis will direct scientists at 16 centers who will study a total of 200 patients for up to 5 years.

Patients enrolled in the study will be randomly assigned to a group receiving either (a) prednisone and cyclophosphamide, or (b) plasmapheresis plus prednisone and cyclophosphamide.

Prednisone is a steroid drug usually used to treat lupus nephritis. Cyclophosphamide, a drug that has a toxic effect on body cells, is often used in an effort to preserve functioning of the kidneys by immunosuppression.

Scientists hope that this carefully controlled study will provide valuable information about the effectiveness and feasibility of plasmapheresis as a treatment for lupus nephritis; the relationships between various tissue abnormalities and responses of patients to therapy, and the mechanism of action of plasmapheresis in lupus nephritis, if the treatment is found to be beneficial.

For more information, contact the NIADDK Office of Health Research Reports, 496-3583. □

New Literature Searches Available From NLM

Five new Literature Searches are available from the National Library of Medicine's Reference Section:

LS 82-15 *Cisplatin*. January 1980—July 1982, 255 citations.

LS 82-16 *Failure to thrive*. August 1977—July 1982, 184 citations.

LS 82-17 *Total hip replacement*. January 1979—August 1982, 173 citations in English.

LS 82-18 *Drugs and pharmacy in developing countries*. January 1977—August 1982, 172 citations.

LS 82-19 *Drug therapy for leprosy patients*. January 1980—August 1982, 135 citations.

These Literature Searches, part of a series of printed bibliographies on subjects of current interest, were produced through NLM's computer-based system, MEDLARS. They are available without charge.

A complete list of available titles appears in each issue of *Index Medicus* and *Abridged Index Medicus*.

When requesting searches, please include title and number, enclose self-addressed gummed label, and mail to: Literature Search Program, Reference Section, National Library of Medicine, Bethesda, Md 20209. □

Awards Index Published

The 21st edition of the *Research Awards Index*, containing scientific data on more than 20,000 Public Health Service grants and contracts active during FY 1981, is now available.

The *Index* is published in two volumes. The first volume contains about 7,000 subject headings under which appear the identification numbers and titles of pertinent projects.

Volume II contains project identification data including the names of investigators, their addresses and project titles; a separate section on research contracts; and an alphabetical list of grantee investigators.

Copies of *Research Awards Index*, (NIH Publication No. 82-200) may be obtained by writing to the Superintendent of Documents, U.S. Government Printing Office, Washington, D.C. 20402. The price is \$26 domestic prepaid, or \$32.50 foreign postpaid. The stock number is 017-041-00134-3. □

The saddest failures in life are those that come from not putting forth the power and will to succeed.—E. P. Whipple □

New Book Depicts History of NLM

A new book, *A History of the National Library of Medicine* by Dr. Wyndham D. Miles, is now available from the Government Printing Office.

Published by the National Library of Medicine, this 469 page volume, including an extensive index and over 100 illustrations, traces the evolution of "our nation's treasury of medical knowledge."

From its birth in 1818 with only a few med-



From 1862 to 1866 the Library's collection remained part of the Surgeon General's office. The office was located on the second floor of the Riggs Bank building on the right. The collection which consisted of works on anatomy, physiology, fevers, diseases of children, dentistry, epidemics, pharmacy, midwifery, medical jurisprudence, and military surgery were shelved in the front parlor of the house on the left.

ical books, the Library's collection has grown to over 2½ million items today.

One figure prominent in the transformation and development of this world famous medical research institution was Army Surgeon Col. John Shaw Billings.

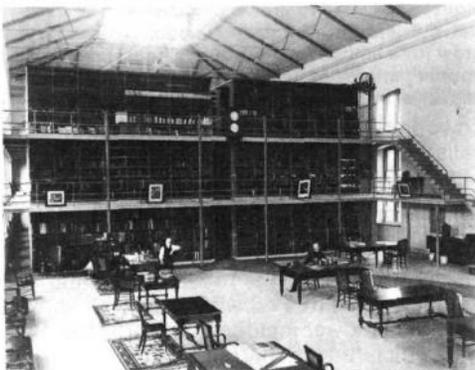
Dr. Billings was appointed librarian in 1865 to what was then known as the Library of the Army Surgeon General's Office. Before his retirement from the Army in 1895, he had

developed the largest and most diversified medical collection in America, perhaps the world.

The Library has seen many homes before becoming part of the NIH campus in 1962. It was originally housed in the Surgeon General's Office, Wash., D.C., and then transferred to Ford's Theater in 1866. In 1887, it was moved into the Library-Museum Building, which was located on the south side of the Mall.

The author, Dr. Miles, is a well-known writer on the history of chemistry and has been an historian at NIH since 1962. He is presently on the staff of NLM's History of Medicine Division.

This first comprehensive history of the NLM is available for \$14 from the Superintendent of Documents, U.S. Government Printing Office, Wash., D.C., 20402. Stock No., 017-052-00224-4.



Moving to the Library-Museum building provided relief from the inadequate facilities in the library at Ford's Theatre in 1887. Working at a table (right) is Dr. John Shaw Billings. The Hirshhorn Museum now stands on the site the library occupied.

opment of a comprehensive description of the clinical patterns of non-Hodgkin's lymphoma.

A native of Shelbyville, Ill., he graduated from Yale University in 1961, and received his medical degree from Harvard Medical School in 1965. Dr. Chabner has received many honors including Pfizer lectureships in clinical pharmacology at the University of Vermont in 1980 and Yale University in 1981. □

Women on the Run!

Women on the Run, an organization promoting women's fitness, offers two levels of running classes at NIH. Level 1 is for beginners with emphasis on pulse-taking, correct form, stretching exercises, diet, injury prevention and setting up a personal running schedule.

Classes are being held on Tuesdays and Thursdays, beginning Sept. 28 at 5:30 p.m. Cost is \$30 for the 3-week class.

Level II is a program designed to help endurance, speed and strength. Classes will meet on Monday and Wednesday evenings at 5:30 p.m., beginning Oct. 4. Cost is \$40 for the 4-week program. The first class for both sessions will meet in Conf. Rm. 4, Bldg. 31.

To register, call 251-0043 or 279-9393 or R&W Activities Desk. □

Three Win Award for Collaborative Paper



The authors (l to r): Mr. Fiori, Ms. Swyt, BEIB, and Mr. Gorlen, CSL, surround their award-winning image, which depicts background-corrected distribution of two elements, illustrating the application of their techniques.

Charles E. Fiori and Carol R. Swyt, physicists in the Biomedical Engineering and Instrumentation Branch, DRS, and Keith E. Gorlen of the Computer Sciences Laboratory of DCRT, have won the McRaes Memorial Award for a paper presented at this year's joint national meeting of the Electron Microscopy Society of American and the Microbeam Analysis Society.

The award is given for a significant contribution to the physics and engineering of electron optical instrumentation.

Describes Image

The winning paper, entitled "Continuum Correction of X-ray Area Scans," describes a mathematical algorithm and electronic modification of an electron microscope that permit the formation of X-ray images with the contribution from continuum X-rays removed.

The image produced is a true representation of the concentration of a particular atomic species with none of the potentially misleading artifacts arising from courses such as irregularities in specimen thickness.

The research that resulted in this award was done at the new BEIB analytical electron microscope facility in Bldg. 13. The 200 keV computerized microscope was developed jointly with the Computer Systems Laboratory of DCRT and is available to the NIH scientific community for collaborative research. Contact C. E. Fiori, 496-2599 for information. □

Evening Speechcraft Offered

An 8-week evening speechcraft course will be conducted by the Kensington Toastmasters Club, an affiliate of the NIH Toastmasters Club, starting Oct. 6.

Speechcraft participants will learn impromptu speaking, various styles of speaking, and how to listen and evaluate.

The cost for the course, which takes place on Wednesday evenings from 7 to 9 p.m. at the Kensington Fire Station, is \$10. For further information, call Dr. Kent Bailey, 496-5905 or Raji Sarma, 949-5775. □

DR. CHABNER

(Continued from Page 1)

From 1976 to 1980, he was chief of the Clinical Pharmacology Branch in the Clinical Oncology Program of DCT, and the following year became associate director of the Clinical Oncology Program and deputy clinical director of NCI. In 1981, he was also named acting director of DCT.

While studying antimetabolites, Dr. Chabner and colleagues at NCI developed methods for measuring drug levels in human plasma.

During the mid-1970's in their research on methotrexate, an important anticancer drug, Drs. Chabner and Robert Young, of NCI's Medicine Branch, described for the first time the relationship between drug concentrations in plasma and the drug's toxic effects on cells. This work established a prototype for cancer pharmacology.

The research provided a means of predicting toxicity and a tool to design more effective and safer treatment plans. Dr. Chabner is the editor of the first textbook in this field of cancer pharmacology, *Pharmacologic Principles of Cancer Treatment*, which was recently published.

Another special research interest of Dr. Chabner and colleagues has been the devel-

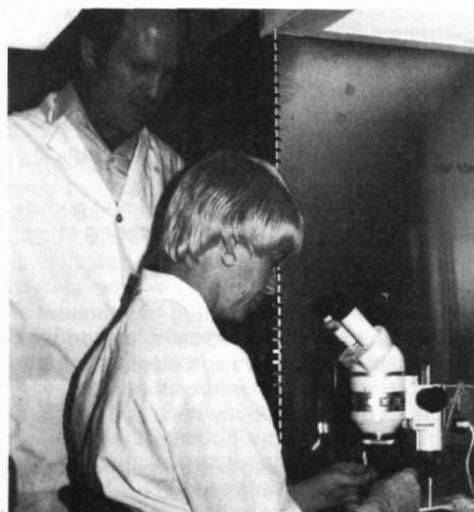
Chemical, Drug Exposure Linked to Cleft Palate

Approximately 1 in every 500 births in the U.S.—10,000 infants each year, suffer from cranial or facial malformations—usually cleft lip or palate.

Dr. Robert M. Pratt, research chemist at the National Institute of Environmental Health Sciences, is among the nation's leading researchers on the biochemical mechanisms of birth malformations, especially cranial-facial defects. He points out that these malformations most often occur when the mother and embryo have a genetic predisposition, and when certain environmental factors such as chemical or drug exposure are present.

He began his research on cleft palate at the National Institute of Dental Research in 1970. Since 1980 he has headed the experimental teratogenesis section within the Laboratory of Reproductive and Developmental Toxicology at NIEHS. Teratology is the study of birth defects.

Various drugs and environmental chemicals are administered to pregnant mice by Dr. Pratt and his research team to ascertain



Dr. Pratt works with Eugenia F. Goulding, a biologist, in their laboratory investigating the normal development of animal embryos and the mechanism of facial and palatal clefting.

the types of induced birth defects. For direct observation, early mouse embryos are grown in culture for 2 days where their development can be closely studied.

In addition, human cell cultures grown from tissues obtained from abortuses (fetuses with no chance of survival) or during corrective surgery of cranial-facial malformations, supply an invaluable approach to understanding basic mechanisms of growth control and how defects are triggered.

"Hormones, specifically glucocorticoids (cortisone for example) are essential in the normal development of the embryo and fetus," Dr. Pratt said. "A certain level of glucocorticoid and its receptor is required, yet more than that level will cause cleft palate to occur."

Epidermal growth factor (EGF) is a small protein that influences certain aspects of the developing embryo and fetus, and apparently disappears at birth. He and



In the facial and palatal clefting study, to observe the development of the embryo inside the mother, mouse embryos are grown in glassware, in a special nutrient "broth" called media. The embryos grow for a limited time (about 48 hours), and show normal patterns of development as well as the impact of exposures to environmental chemicals.

coworkers have shown that many developing cells are highly dependent on the presence of EGF and that an embryonic type of EGF is likely produced by a number of embryonic tissues including the palate.

Another exciting direction in the lab's research uses vitamins to reduce clefting. Pregnant mice treated with vitamin B⁶ show a markedly lower incidence of cortisone-induced clefting in their offspring.

"This research and its possible clinical implications must be interpreted with great care," Dr. Pratt cautioned, "because too much of any chemical, even a vitamin or growth factor, may harm the development of the embryo or fetus."

The NIEHS researcher is in frequent contact with scientists in the National Toxicology Program, HHS, to keep them updated on progress in the development of methods for culturing human cells and its potential use in birth defect and toxicity testing. □



A summary of the proceedings from the International Symposium on Measles Immunization held in March 1982 has been written by Dr. Samuel L. Katz of Duke University Medical Center. Dr. Katz was the senior rapporteur for the symposium which was coordinated by the Fogarty International Center. Reprints of the complete symposium can be obtained from Dr. Earl C. Chamberlayne, FIC.

Dr. Stephen Marx Wins F. Albright Award

Dr. Stephen Marx, senior investigator, Metabolic Diseases Branch, NIADDK, is a 1982 recipient of the Fuller Albright Award of the American Society for Bone and Mineral Research.

The award, given at the society's annual meeting in June, honors an outstanding young investigator under the age of 40. Dr. Marx shares the honor with Dr. Gregory Mundy, Veterans Administration Hospital, San Antonio, Tex.

Dr. Marx's research has focused on the hereditary abnormalities in mineral metabo-



Dr. Marx has authored more than 90 scientific papers, is a member of several societies, and is on the editorial boards of two professional journals.

lism, particularly in familial hypocalciuric hypercalcemia, and also on receptors for calcitropic hormones.

He has described a new radioimmunoassay for the middle region of human parathyroid hormone, a technique that is an improvement over previous methods.

Dr. Marx received his M.D. degree from Johns Hopkins Medical School in 1968 and a B.A. degree from Yale College in 1964. He came to NIADDK in 1970 as a clinical associate. With the exception of a 1-year residency at Massachusetts General Hospital, Dr. Marx has been with the Institute since. □

Healthy Volunteers Needed For Light Effects Study

Healthy volunteers, both male and female, ages 20-55, are needed for a light effect study by the National Institute of Mental Health.

Participants are required to follow certain dietary practices, give urine samples, and fill out forms at intervals for a period of 1 year. Compensation will be provided.

For further information, contact Connie Carpenter, 496-2141. □

A fanatic is one who can't change his mind and won't change the subject—Sir Winston Churchill □

Dr. Donald Jerina Receives Brodie Award

Dr. Donald Jerina, chief of the section on oxidation mechanisms, NIADDK, received the Bernard B. Brodie Award in drug metabolism on Aug. 16 at the annual meeting of the American Society of Pharmacology and Experimental Therapeutics in Kentucky.

The award was established by the Ciba-Geigy Corporation to honor the fundamental contributions of Dr. Bernard B. Brodie in the field of drug metabolism and disposition. Dr. Brodie served as chief, Laboratory of Chemical Pharmacology, NHLBI, from 1950 to 1970.

The award—\$2,000 honorarium, commemorative medal, and certificate—is presented every 2 years.

Dr. Jerina is the third recipient of the prize. Contributions for which he was cited include the discovery of intramolecular migration of tritium and deuterium during the hydroxylation of aromatic compounds, commonly termed the "NIH shift."

He and his colleagues were the first to trap epoxides as metabolites of aromatic hydrocarbons, thereby providing unequivocal evidence that the liver microsomes contain enzymes that catalyze the formation of epoxides.

Drs. Jerina and John W. Daly also discovered epoxide hydrolase, an enzyme which catalyzes the conversion of arene oxides into trans-dihydrodiols.

Dr. Jerina is also known for his work on the Bay-Region Theory, performed with colleagues at NIH and in collaboration with others at Hoffman-La-Roche.

This theory predicts the sites responsible for mutagenicity of the various polycyclic hydrocarbon oxides and is important in forecasting the carcinogenic potential of hydrocarbon metabolites.



Dr. Jerina also was the 1979 recipient of the Hillebrand Prize from the American Chemical Society and has published nearly 300 papers during his research career.

Current work in the laboratory is aimed at the identification of compounds capable of blocking the tumorigenic activity of polycyclic aromatic hydrocarbons. Ellagic acid, a naturally occurring plant phenol found in such common foods as grapes, tea, and coffee, is one of those compounds.

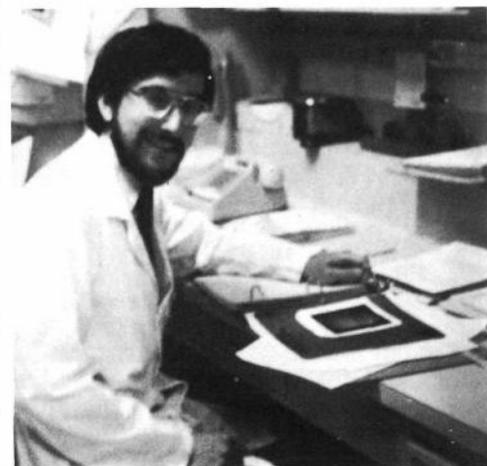
It has been found to be very effective in inhibiting mutagenic activity of the carcinogenic bay-region diol epoxide of benzo(a)pyrene *in vitro*.

Dr. Jerina received his B.A. in chemistry from Knox College in 1962 and his Ph.D. in organic chemistry from Northwestern University in 1966. He joined the NIH as a staff fellow the same year, and assumed his current position as section chief in 1973. □

Dr. David Cohen Wins Leukemia Society Fellowship

Dr. David I. Cohen of the National Institute of Allergy and Infectious Diseases was recently awarded a 2-year, \$30,000 fellowship by the Leukemia Society of America.

Dr. Cohen, of NIAID's Laboratory of Immunology, was chosen for this honor



Dr. Cohen was one of 33 highly skilled researchers selected to receive the fellowship this year, all of whom are at the intermediate or advanced stages of their medical careers.

based on his ability to conduct scientific research into leukemia and related disorders.

During the grant period, which began in July, he will concentrate on immunology research—the study of the body's immune defense system against disease in order to bolster its own natural ability to fight leukemia.

Born in Shaker Heights, Ohio, Dr. Cohen received his M.D. degree in 1977 from Harvard Medical School. He graduated in 1972 from Harvard University with an A.B. degree in biochemistry.

Before joining NIAID, he served his internship and residency in internal medicine at Washington University/Barnes Hospital, St. Louis. □

Free Meditation Lectures Offered

Two introductory lectures on transcendental meditation will be presented by the R&W TM club on Thursday, Sept. 30, at noon, and 4:30 p.m. in Bldg. 31, C-wing, sixth floor, Conf. Rm. 9. For further information, call John Knight, 496-5361. □

I have never been hurt by anything I didn't say.—Calvin Coolidge □

Short-Term Toxicity Tests Key Goal of NIEHS Studies

Development of inexpensive, accurate, and rapid testing to determine whether or not environmental agents have potential for causing heritable mutations, other kinds of toxicity, or cancer, is a key goal of the National Institute of Environmental Health Sciences.

This research area falls under the National Toxicology Program of HHS. Dr. Raymond W. Tennant, chief, Cellular and Genetic Toxicology Branch, is responsible for developing these short-term test systems.

The NIEHS scientists quickly emphasize that cancer causation is not an either/or proposition and not a single disease but a group of diseases. Two alternative concepts of cancer causation fundamental to developing model tests are to be evaluated; the first involves gene mutation, the second, other genetic damage including aneuploidy (mismatched number of chromosomes), and recombination of gene translocations.

"Perhaps the most dominant and universally acceptable theory of cancer causation," Dr. Tennant said, "centers on the mutation theory that an outside agent induces a change in genes, and given certain other factors, a tumor arises."

This theory has been used in developing bacterial tests for mutagenicity, as a screening tool for predicting carcinogenicity, and for selecting agents for further study. The most commonly employed test uses *Salmonella* bacteria and was developed by Dr. Bruce Ames of the University of California at Berkeley, whose work is supported in part by NIEHS.

At NIEHS, Dr. Errol Zeiger has further developed the *Salmonella* test for screening environmental substances for mutagenicity.

Dr. Henrich V. Malling, Laboratory of Genetics, has been investigating mutagenesis in mammalian organ systems for nearly 20 years. His laboratory has developed a method of detecting mutant cells using fluorescent molecules to flag antibodies.

Dr. Malling is one of the founders of the Environmental Mutagen Information Center sponsored by NIEHS at the Oak Ridge National Laboratory in Oak Ridge, Tenn.

"The second theory proposes that some cancers arise through alteration of gene regulation," Dr. Tennant said. "There is particularly good evidence of this for skin cancer and for leukemias which arise from formative or stem cells. This proposes that the cell has an innate tendency that may be triggered by time alone."

Interest in short-term testing and validation is worldwide. A recent major international effort in short-term testing evaluated 25 tests involving 42 substances, both known carcinogens and noncarcinogens. The U.S. representative on the study's coordinating committee was Dr. Frederick de Serres, NIEHS associate director for genetics.

Various test systems based on alternate theories of carcinogenesis will be further developed by NIEHS as a test battery for screening substances to determine which chemicals should be selected for long-term (2-year) tests using laboratory animals. □

Metabolism Study on Chinese People Suggests Genetic Processing Difference



L to r: Drs. Chang, Rudorfer, Potter, Lane and Zhang compared the metabolic rates of visiting Chinese scientists with American Caucasians to evaluate hydroxylation of tricyclic antidepressant drugs.

A genetic difference in metabolism apparently accounts for the use of lower doses of tricyclic antidepressant drugs in China than in the West, according to National Institute of Mental Health scientists.

An intramural study has confirmed earlier suspicions that the breakdown of such drugs by enzymes in the liver—a process called hydroxylation—tends to be slower among Chinese than among Caucasians, suggesting probable hereditary differences.

One of the first substantive outgrowths of the U.S.-China Cooperative Agreement on Health, the study at NIMH employed visiting scientists from China as both investigators and subjects, and was conducted on campus.

In collaboration with Drs. Mingdao Zhang and Wen-Ho Chang, visiting scientists at NIMH under the 1980 agreement, Drs. William Potter and Mathew Rudorfer of NIMH's Clinical Psychobiology Branch, and Dr. Elizabeth Lane, a visiting fellow from Australia, compared the metabolism of a single dose of desipramine in a sample of 16 Americans and 14 Chinese. Most of the latter were NIH visiting scientists.

Traces of the drug and by-products of its breakdown were measured daily in blood and urine samples over a 5-day period. The substances took longer to clear the body among the Chinese.

This suggests that genes determining rates of hydroxylation for the large class of drugs represented by desipramine are expressed according to a "trimodal" distribution.

"Some Chinese are slow and some are intermediate. Some Caucasians are rapid and some intermediate. But very rarely are Caucasians slow or Chinese rapid in hydroxylation rates," explained Dr. Lane.

The slower metabolic activity results in relatively higher levels of the drugs remaining in the body, and hence requires a lower dosage, said Dr. Rudorfer.

Dr. Potter added that the finding will permit development of predictive tests for tailoring drugs to the requirements of different populations. Use of tricyclics as neuroendocrine probes may also help resolve a question about the prevalence of depression in China.

Refinement of such knowledge into predictive tests of drug response promises a shortcut to determining dosages for the large and growing array of cardiovascular and psychoactive drugs that are metabolized by hydroxylation, noted Dr. Potter.

Without such a theory or model, proper dosages for each new drug could be determined only by painstaking and sometimes risky trial and error over times in each population.

Research psychiatrists are also intrigued by the prospect of using desipramine response as a biological marker for depression in China. Americans diagnosed as depressed show a characteristic biochemical abnormality, blunted growth hormone levels, after a single dose of the drug.

Drs. Zhang and Chang now will be able to train other Chinese investigators in how to perform the growth hormone assay and to carry out the clinical protocol. They plan to screen Chinese patient populations for the abnormal desipramine response upon their return to China.

Dr. Potter hopes the studies will eventually help determine the prevalence of depression in China. Chinese psychiatrists, particularly in the northern province, report surprisingly few cases of depression, perhaps due to different diagnostic schemes or social stigma surrounding the illness.

"We need to compare populations across symptoms, taking a neutral view, free of language issues, and simply ask: Are biological markers which are abnormal in Caucasian depressives also abnormal in Chinese?" said Dr. Potter.

—Jules Asher □

New Sequencing Data Bank Will Start in Los Alamos

A 5-year, \$3.2 million contract, coordinated by the National Institute of General Medical Sciences, has been awarded for the purposes of creating and maintaining a new data bank on base molecules in nucleic acids.

In recent years, modern techniques for analyzing nucleic acids have led to an explosion of data concerning the composition of DNA and RNA molecules.

These data are crucial to understanding the complex genetic information held by DNA and transmitted by RNA to cell structures where life processes are carried out.

The sequences (or order) of some 750,000 base molecules in several hundred nucleic acids have been determined—a number that may grow at an exponential rate in the near future.

Bolt Beranek and Newman, Inc., of Cambridge, Mass., prime contractor, will collect, organize and supply data in this rapidly growing area. The company is collaborating with the Los Alamos National Laboratory, where a pilot project to collect nucleic acid sequences has been active over the past 3 years.

BBN will distribute information to subscribing institutions and scientists via magnetic tape, an annual printed compendium, and limited computer-based online access.

Researchers at Los Alamos will gather, annotate, and organize the data. Readily available sequence information will help scientists, particularly geneticists and molecular biologists, build a foundation for further advances in biomedical research.

Cosponsors of the new data bank project are NIGMS, the National Institute of Allergy and Infectious Diseases, the National Cancer Institute, the Division of Research Resources, the National Science Foundation, the Department of Energy, and the Department of Defense.

Coprincipal investigators are Dr. Howard Bilofsky of BBN and Dr. Walter Goad of the Los Alamos National Laboratory. □



The National Eye Institute recently presented special achievement awards to public information specialist Claudia S. Feldman (r) and editorial assistant Margaret W. Strock. The two Office of Scientific Reporting staff members were recognized for their vital role in planning and carrying out an NEI information project to disseminate findings from the Senile Macular Degeneration Study.

Rimantadine Found 'Drug of Choice' For Preventing Influenza A Infection

Two related drugs, amantadine and rimantadine, effectively protect against influenza A infection, but rimantadine produces significantly fewer side effects, according to a recent study.

These results suggest that rimantadine is the drug of choice for prevention from influenza A. Until now, the effectiveness of rimantadine had not been documented in a strictly controlled, large clinical trial.

Amantadine has been approved for prevention and treatment of influenza A since 1976, but has not been widely used. Rimantadine is approved only for experimental use although it is used abroad, particularly in the Soviet Union.

In this study with young, healthy volunteers, both drugs were effective, but amantadine produced more central nervous system side effects, mainly insomnia, jitteri-

ness, and difficulty in concentrating. The side effects disappeared however, within 48 hours after medication was discontinued.

Scientists at the University of Vermont College of Medicine began their study during the early stages of a 1981 influenza outbreak in Burlington, Vt. Four hundred and fifty volunteers, aged 18 to 45 years, were enrolled in a controlled double-blind trial.

Study participants were given tablets twice a day for 6 weeks. One-third received amantadine; one-third received rimantadine; and one-third received a placebo, an inactive substance.

No Symptoms Evident

Both rimantadine and amantadine were effective in preventing influenza-like illness, defined as a cough and/or fever, and at least two of the following symptoms—sore throat, headache, or muscle aches.

When compared with placebo, rimantadine reduced the rate of illness 65 percent, and amantadine reduced the rate 78.2 percent.

The effects were even more striking when the investigators analyzed the reduced rates of laboratory-confirmed influenza A illness. Rimantadine decreased this rate by 85.4 percent, and amantadine lowered the rate by 91.2 percent, when compared with placebo.

These findings also indicate that some influenza-like illnesses were not caused by influenza A viruses, but by other organisms not receptive to these medications.

Flu Virus Vaccine Available to Employees

CNS side effects developed in 13.1 percent of the volunteers receiving amantadine, 6.1 percent of rimantadine recipients, and 4.1 percent of placebo recipients. The frequency of other side effects, such as gastrointestinal problems, was the same for all groups.

CNS side effects were responsible for a higher rate of withdrawal by amantadine recipients from the study. (Of amantadine recipients, 22.1 percent withdrew, compared with 10.8 percent of placebo recipients, and 9.5 percent of rimantadine recipients.)

Laboratory tests on all volunteers revealed that several had evidence of influenza A infection even though they had had no symptoms of illness. Both drugs seemed less effective in preventing infection with influenza A virus than in preventing infection-associated illness.

Compared with placebo, rimantadine reduced the rate of infection 65.7 percent. Amantadine reduced this rate 74.4 percent. This phenomenon may be desirable, however, if these subclinical (inapparent) infections provide immunity to subsequent infections with the same or related influenza A viruses.

The scientists recommend that additional studies be done to determine whether results, including the low rate of side effects, would be similar in elderly or other high risk persons.

This study was supported by contract from the National Institute of Allergy and Infectious Diseases. The investigators, Drs. Raphael Dolin, Richard C. Reichman, H. Paul Madore, Raina Maynard, R.N., Pamela M. Linton, R.N., and Joan Webber-Jones, R.N., reported their findings in the Sept. 2, 1982, issue of the *New England Journal of Medicine*. □



Time-Life Books recently expressed appreciation to the various NIH information offices for assistance provided during 1981 in the preparation of their Library of Health series. The Parents of Preschoolers, Inc., daycare centers for children of NIH employees, received a \$1,000 gift, which NIH Deputy Director Dr. Thomas E. Malone (r), presented to Sherrie Ruddick, NIH Preschool Developmental Program director.

Dr. Donald Whedon Honored at Farewell Party

Dr. G. Donald Whedon, senior scientific advisor, NIADDK, and former Director of the Institute was recently honored at a farewell party given in his honor by former staff members.

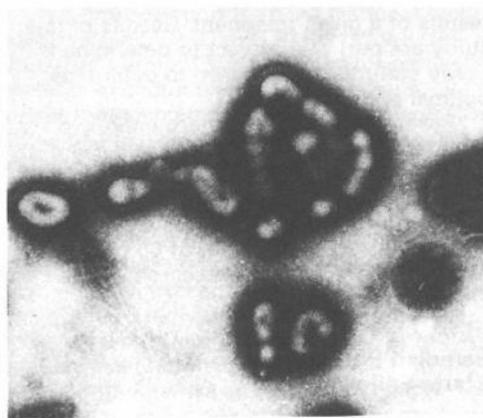
At the party, Dr. Whedon announced that on Oct. 4, he will be going to the Kroc Foundation in Santa Barbara, Calif., as a senior associate and director of their conference program. In addition to his duties at the foundation, Dr. Whedon will have an appointment as adjunct professor of medicine at UCLA.

Dr. Whedon said that he has mixed feelings about moving on since the Institute has been like a family to him.

"I really appreciate the show of affection I have received over the past years and I hope your new Director, Dr. Lester B. Salans, will receive the same."



Sally L. Nichols, former secretary to Dr. Whedon, presented him with a certificate during the farewell party proclaiming their former Director "number one" in their opinion.



The influenza A virus examined by the Centers for Disease Control in 1977 is magnified 118,000 times in this photo.

ness, and difficulty in concentrating. The side effects disappeared however, within 48 hours after medication was discontinued.

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These findings also indicate that some

Medical, Dental Students Complete First CC Summer Research Fellow Program

Fifty-two medical and dental students from various parts of the country recently ended their participation in the first NIH Summer Research Fellowship program.

Sponsored by the Clinical Center, the students conducted research in selected areas of laboratory investigation and attended lectures and seminars to enhance their education and develop investigative skills. The program is designed to make medical students aware of NIH research programs and provide them with quality laboratory training.

It is hoped that the program will boost the number of medical professionals who choose research as a career. "To develop scientific leadership, it is vitally important to introduce outstanding medical students to research programs early in their medical training," said Dr. Jay R. Shapiro, Acting CC Director.

This may prove of exceptional value in terms of helping NIH to maintain an applicant pool of quality physicians who aspire to careers in academic medicine," he added.

The fellows were chosen from more than 300 applicants to work in one of seven Institutes participating in the program. They were each assigned preceptors who directed their research projects.

James Alexander, CC EEO coordinator, organized the program and arranged a publicity effort that included sending notices about the program and brochures to students, as well as personal visits to medical and dental schools.

Philip Krause, a third-year medical student at Yale University from Urbana, Ill., became aware of the program when he received a brochure in the mail.

"I wanted to go into research, but I'd never worked in a lab," he said. "I thought this would be a good opportunity." Mr. Krause completed his undergraduate work and received a master's degree in computer science from the University of Chicago. He has found the program beneficial.

"It has been an excellent experience," he said. "It has given me the basis for the type of thinking needed to be a research scientist and a good background into NIH."

Sponsored by the National Institute of Allergy and Infectious Diseases, Mr. Krause worked on hybridization of viruses, which involves combining strands of DNA from different virus particles in the hope of developing rapid diagnostic techniques for virus infections.

Garry Millard, a first-year dental student at the University of Minnesota from Great Falls, Mont., found the program a positive experience.

He considers it well organized and functional and particularly enjoyed the Wednesday afternoon seminar speakers—such as Dr. Julius Axelrod, an NIMH Nobel Prize winner.

Mr. Millard's research project centered on testing basophilic leukemia cells for histamine release, and the role of calcium flux which is required for histamine release in the cells. He developed an experiment that uses radioactive calcium to monitor the



Mr. Millard worked with NIDR testing basophilic leukemia cells.

efflux of calcium from the cells.

Mr. Millard completed his undergraduate work at Montana State University in Bozeman. He fulfilled his fellowship with the National Institute of Dental Research. As his first experience in Washington, he has enjoyed many of the cultural and recreational aspects of the area along with his scientific training.

Neither the Washington area nor NIH are new to Lisa Battle, a summer research fellow with the National Institute of Neurological and Communicative Disorders and Stroke, who is a third-year medical student at Howard University.

From Lothian, Md., Ms. Battle previously worked in the Baltimore Cancer Research program in microbiology and neurology. This summer she conducted both clinical and laboratory research.

"The program has been designed so that we're not just another pair of hands, we're actually getting research under our belts," she said. "It has been excellent—the lab experience has been very positive," Ms. Battle said.

Her work this summer involved determining chemotherapy sensitivity on patient



Ms. Battle did both clinical and laboratory research with NINCDS during her fellowship program.



Mr. Krause was sponsored by NIAID and worked on the hybridization of viruses in an effort to develop techniques to detect viral infection.

brain tumor cells taken from surgical specimens and grown in tissue culture.

She then used a computer to determine results of a given treatment. Results of this study are part of a project to determine if tissue cultures can be used to determine optimal patient treatment.

"Research and dentistry are entirely different disciplines." Mr. Millard said, "and it's too early for me to decide between the two."

"But this experience has opened my eyes to the fact that research is available as an alternative career. A career of 60 percent practice and 40 percent research seems like a nice combination." □

Swedish Pediatrician Starts Fellowship

Dr. Steffan Cullheim, a pediatrician at the Huddinge Hospital, Karolinska Institutet, Stockholm, Sweden, began a Fogarty International Center research fellowship on Sept. 3.

He will be under the preceptorship of Dr. Robert Burke in the Laboratory of Neural Control, NINCDS. The title of his research project is Studies on Excitatory Synaptic Inputs to A-Motoneurons. □



Trudy Axilrod, former technical information specialist in the Division of Research Grants, retired Aug. 27 after 20½ years of service at NIH. She receives congratulations and best wishes from William Holliman, chief, Research Documentation Section, Statistics and Analysis Branch, DRG.

Aluminum: An Insidious Contribution to Alzheimer's Disease?

A major new finding reported in the Sept. 10 issue of *Science* has linked the results of two separate avenues of research on Alzheimer's disease—research that suggests that aluminum may contribute to the disease's development, and research that probes the excess incidence of dementia in three separate populations. Alzheimer's disease is the most common form of "senility" among the elderly.

In a decade marked by major advances in the fields of neuroscience and aging research, scientists have employed a variety of methods to investigate the possible cause(s) of Alzheimer's disease.

Their studies have looked at the roles of heredity, trace metals, deleterious changes in brain chemistry, and slow-acting viruses, as well as the effect of changes in the aging immune system.

This latest finding focuses on the hallmark of Alzheimer's disease, the presence of tangled fibers in the brain cells of victims.

With grant support from the National Institute on Aging, Dr. Daniel P. Perl of the University of Vermont has extended his earlier findings of accumulations of aluminum within the affected nerve cells of subjects showing the classic neurofibrillary tangles of Alzheimer's dementia.

Dr. Perl and Drs. D. Carleton Gajdusek, Ralph M. Garruto, Richard T. Yanagihara, and Clarence J. Gibbs, Jr., of the NINCDS report the new finding of high accumulations of aluminum, iron and calcium in the brains of Chamorro natives of Guam who have died of amyotrophic lateral sclerosis (ALS) or parkinsonism-dementia.

This population is adversely affected by these two chronic disorders, both of which were previously suspected to be transmitted by a slow-acting virus.

For several years, Dr. Gajdusek and his NINCDS colleagues have been studying the possible implications of Guam's environmental deficiency in calcium and magnesium and excess of aluminum and other metals.

Aging researchers have kept a watchful eye on studies in Guam because of the sim-



Aluminum is one of the most abundant of the Earth's elements. It is in the air, in the soil in which foods are grown, as well as in certain commercial products. It may be that high intake of aluminum over a long period of time, coupled with chronic low intake of vital minerals, such as calcium and magnesium, ultimately leads to Alzheimer's disease, particularly among the elderly.

ilarities between the parkinsonism-dementia syndrome and the presenile form of Alzheimer's dementia. In both disorders, there is an excessive accumulation of neurofibrillary tangles in the brains of victims that is associated with severe dementia and death.

These latest findings reconfirm Dr. Perl's earlier work in support of studies linking high concentrations of aluminum in the brain to the development of neurofibrillary tangles, as well as work of Japanese investigators in both Guam and Japan.

They also lend support to a developing hypothesis that environmental factors may be an underlying cause of the ALS and dementia so prevalent in Guam.

NINCDS scientists are exploring the possibility that secondary hyperparathyroidism caused by lack of calcium and magnesium in

the environment provokes an accumulation of metal ions within brain tissue.

Samples of garden soil and drinking water in Guam, as well as in parts of Japan and New Guinea that are similarly plagued by high incidences of ALS and dementia, indicate low levels of calcium and magnesium and unusually high levels of aluminum.

Scientists have never been able to prove that aluminum alone predisposes a person to, or causes, Alzheimer's disease.

Future studies will determine whether accumulations of metals in the brain are a primary cause of Alzheimer's disease, or if other factors or circumstances might combine with environmental factors to trigger the onset of chronic, but ultimately fatal, diseases of the nervous system. □

Roger B. Mack Made CC Program Coordinator for NIH Nursing Unit

Roger B. Mack, former chief of the respiratory therapy section of the Critical Care Medicine Department of the Clinical Center, was recently selected as a program coordinator.

CC program coordinators work closely with the medical and nursing staff on the patient care units. They have assumed many administrative duties previously taken care of by the nursing staff, allowing nurses more time for direct patient care. These duties include monitoring the unit's safety and environment, and planning unit design and renovation.

They were also responsible for the unit's supply levels and equipment. Mr. Mack will be responsible for coordinating all the nursing units for the National Institute of Mental Health.

He came to the CC as a respiratory therapist in 1966. He was appointed chief of that section a year later and since then has built



After a 2-week training period, Mr. Mack began his new job as nursing program coordinator for NIMH Sept. 7.

up the area considerably. It now has 12 respiratory therapists, compared with only three when he first came to the CC.

As a nursing student, Mr. Mack became interested in the mechanics of respiratory therapy. He was certified as a respiratory therapist by the National Board of Respiratory Therapy and has been a member of the American Association for Respiratory Therapists since 1963. □

OMS Presents Program on Friendship

The Employee Assistance Program of the Occupational Medical Service, Division of Safety, will present a program called Friendship: The First Relationship on Monday, Oct. 4, in Bldg. 31, Rm. B3C02C from noon to 1 p.m. For further information, call Morris Schapiro, 496-3164. □

Pigeon Breeders' Disease Study May Create Lung Disorders Model

The triggers of allergic lung diseases are in the home and in white collar businesses, in grain silos and in freight cars, even in pigeon cotes.

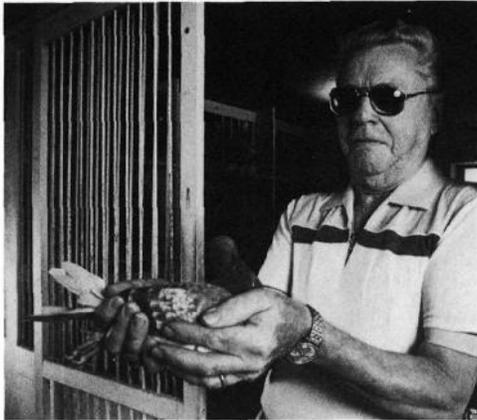
Regardless of the source, the effects are always the same—impaired breathing, coughing, fever, and chills—the symptoms of a broad class of disorders called hypersensitivity pneumonitis.

Some people exposed to these allergens develop symptoms and others do not. The reason, according to researchers at the Medical College of Wisconsin in Milwaukee, is that some people maintain a natural defense, cells that specifically suppress the effects of allergens.

When these cells—suppressor T-lymphocytes—fail to suppress the immune response, antibodies and sensitized cells attack and damage lung tissue, leading to the symptoms of hypersensitivity pneumonitis, says Dr. Jordan Fink, chief of the allergy and immunology section in the MCW department of medicine.

In studying pigeon breeders' disease, a lung allergy caused by inhaled pigeon matter, Dr. Fink and his colleagues discovered that a population of suppressor cells is active in the blood of healthy pigeon breeders, but not in the blood of patients with symptoms of the allergy.

Although pigeon breeders' disease affects only a small number of people, it may be a model for all forms of hypersensitivity pneumonitis. The symptoms are identical for all types of this disorder, Dr. Fink has found. A variety of bacteria, fungi, and protozoa can cause it



Carl C. Gill, Milwaukee pigeon breeder, has been very cooperative in recruiting fellow breeders to participate in allergy tests at the Division of Research Resources-supported General Clinical Research Center.

blood of asymptomatic subjects than in the blood of patients with the clinical signs of the disease.

Dr. Fink believes this heightened activity in asymptomatic subjects occurs throughout the body. If his hypothesis proves to be correct, the research may lead to an effective treatment or cure for hypersensitivity pneumonitis.

The study of pigeon breeders' disease is being funded primarily by the National Heart, Lung, and Blood Institute, the National Institute of Allergy and Infectious Diseases, the Division of Research Resources, and the Veterans Administration.

The only effective treatment currently available for the disease is the use of corticosteroids, which can cause hypertension, decalcification of bone and numerous other adverse effects when used for a long time.

To make management even more difficult, neither avoidance nor treatment with corticosteroids is always enough. Symptoms may persist in some patients, leading to chronic lung disease, which reduces the patient to a "pulmonary cripple," says Dr. Fink.

With pigeon breeders' disease as a model, the Milwaukee researchers hope to understand the defect that inactivates suppressor cells and makes people susceptible to allergens.

Patients with pigeon breeders' disease show clear-cut signs of the disease, thereby simplifying the diagnosis. Willing pigeon breeders participate in the research, providing financial support through their national organization and traveling across the nation to the DRR-supported General Clinical Research Center in Milwaukee.

In continuing their study of the disease, the first priority of Dr. Fink and his colleagues is to design a screening method for identifying susceptible individuals.

Their next priority is to design a therapy, one that will reactivate the protective mechanism that is dormant in patients with the disease. □



Dr. Fink reports that preliminary evidence suggests that the activity of suppressor T-cells in the lungs of symptomatic pigeon breeders is not adequate to control the immune response to pigeon antigens.

These microorganisms can invade virtually every segment of society. They live in the heating and cooling systems of homes or businesses, contaminating the air breathed by residents or employees.

They may be present in foodstuffs such as grain and malt, exposing farmers and handlers on loading docks and in breweries to airborne allergens.

At present, the hypothesis that the activity of suppressor cells is the major determinant of hypersensitivity pneumonitis in pigeon breeders is primarily supported by tests indicating greater suppressor activity in the

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