High Dose Treatments With Alkylating Agents May Lead to Increased Risk of Leukemia

A study of ovarian cancer patients treated with the anticancer drugs melphalan or chlorambucil has shown definitively that some women treated with high doses of the drugs are at increased risk of later developing acute nonlymphocytic leukemia (ANL).

Some effective anticancer agents are known or are suspected of being cancer-causing agents themselves. A number of studies have shown an association between certain anticancer drugs and development of leukemia years later.

Melphalan and chlorambucil are both alkylating agents, a class of drugs used effectively to treat many forms of cancer. Yet, alkylating agents have been associated with late development of leukemia in some patients treated for Hodgkin's disease, multiple myeloma, and ovarian cancer.

The National Cancer Institute study—published in Dec. 2, 1982, New England Journal of Medicine—confirms previous findings of excess risk of ANL in ovarian cancer patients treated with alkylating agents, and it identifies two specific alkylating agents that may be responsible for this increased risk.

Analyses were conducted on 1,399 women with ovarian cancer who were treated in five randomized clinical trials. Of these women, 998 were given alkylating agents, and 12 of them developed ANL. (The expected number of ANL cases in the

Dr. Ronald Levy Shares Armand Hammer Award

Dr. Ronald Levy of Stanford University Medical Center in Palo Alto, Calif., an NCI grantee, became the first beneficiary recently of an annual prize established by the Armand Hammer Foundation to reward "the person or persons deemed to have made the greatest contribution to the cure for cancer."

Dr. Levy will share the first $100,000 prize with an Australian researcher, Dr. George Stevenson, director of the Tenovus Research Laboratory in England, for their research using polyclonal and monoclonal antibodies in the treatment of human lymphoid malignancies.

Dr. Levy and Stevenson's work concerns leukemia and lymphoma, forms of cancer of the blood and lymph glands.

Dr. Stevenson has shown that leukemia cells of the B-cell type have a substance on their surface, called idiotype, which is not found in normal cells. His group raised conventional (polyclonal) antibodies reactive to idiotype and showed that they could selectively kill the leukemia cells.

Dr. Levy and his colleagues were successful in producing monoclonal antibodies against such idiotypes and are using these antibodies for therapy. When such antibodies were injected into one patient, they led to the regression of his tumor. This

(See ARMAND HAMMER, Page 9)

Dr. Guroff's administrative responsibilities in NICHID included a period when he served as acting scientific director.
Training Tips

The following courses, sponsored by the Division of Personal Management, are given in Bldg. 31.

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Golfers Hold Organizational Meeting

The NIH Golf League will hold an organizational meeting on Feb. 24 at noon in Conf. Rm. 2A, Bldg. 31.

Men and women golfers of all skill levels are encouraged to attend. League members play nine holes once a week after work at Falls Road Golf Course. Team and flight are determined by handicap.

Anyone interested in joining but unable to attend or has further questions may contact Suzanne Stimler, 496-5411. Membership in R&W is required.

STEP Forum on Indirect Costs To Be Presented on Feb. 22

On Feb. 22, the STEP committee will present a forum on Indirect Costs: The What and Why.

Stanley H. Goldrich, principal staff accountant, Division of Contracts and Grants, will speak on what indirect costs are, how they are developed, why there are differences in indirect cost rates among institutions and what the trends are at NIH.

The forum will be held in the Shannon Bldg. (formerly Bldg. 1), Wilson Hall, from 9:30 to 11:30 a.m. Open to all NIH employees, no advance registration or application is necessary.

For further information, call Arlene Bowles, 496-1493.

Madrigal Singers Seek Members

The NIH Madrigal Singers—unaccompanied part-singing of Italian, English, Renaissance, and early Baroque—are seeking new members. Weekly meetings are held in members' homes, and occasionally the group performs in concert, often with the NIH Singers.

Sight-reading experience is preferred but those singers willing to learn are welcome to join.

For further information, call Charles Bacon, 496-4823, or Dick Shrager, 496-1122.

Ample Parking Just a Walk Away

Having difficulty finding a parking space at NIH? The NIH Parking Office has advised that daily there are approximately 300 to 500 empty spaces in lots 16F and 41B (approximately five blocks from Bldg. 10) for NIH employees or visitors.

All NIH parking permits are valid in these areas which include carpool, general and preferential permits.

For further information call the NIH Parking Office, 496-5050.

Free Science Writing Course Offered

A free course entitled Introduction to Scientific Writing and Editing is being given by Dr. A.J. Bachrach, director, Environmental Stress Program Center, Naval Medical Research Institute.

The course will offer a general discussion of writing techniques and style for scientific writers and editors with specific topics presented by guest lecturers.

Limited to 20 students, registration deadline is Feb. 2. The class will be held Wednesdays, Feb. 9 through Mar. 16, from 9 to noon, in the Commanding Officer's Conference Rm., NMRI, Bethesda, MD 20814. For more information and registration, call Regina Hunt, 295-0112.
Building 1 was officially renamed the James A. Shannon Building on Jan. 18 during day-long ceremonies that took on an appearance of a reunion of long-time colleagues and associates.

Coming from far and near, some 500 friends and former colleagues gathered to honor the Director under whom the NIH achieved renown as the world's foremost biomedical research institution.

Among attendees were six past and present NIH Directors—Drs. James B. Wyngaarden, Donald S. Fredrickson, Robert S. Stone, Robert Q. Marston, and William H. Sebrell. Jr. Former PHS Surgeons General Leonard A. Scheele and Luther L. Terry also were present, as were retired NIH personnel, friends, and NIH professional and administrative staff. Also attending were Dr. Shannon's son, Tony, his wife, Kay, and two granddaughters.

Memories Shared

Dr. Wyngaarden, NIH Director, welcomed the invited guests at the 2 p.m. ceremony in the Clinical Center auditorium at which a distinguished panel—including two Nobel laureates—reflected on the early years with anecdotes about how Dr. Shannon brought them to NIH, early research efforts, and the excitement of participating in the growth of NIH.

Speakers were Drs. DeWitt Stetten, Jr., NIH Senior Scientific Advisor; Sidney Underfriend, director, Roche Institute of Molecular Biology; Robert W. Berliner, dean, Yale Medical School.

Also, Drs. Christian Anfinsen, special assistant to the president on new technology transfer, department of biology, Johns Hopkins University; Julius Axelrod, chief, section on pharmacology, Laboratory of Clinical Science, NIMH, and Bernhard Witkop, Chief, Laboratory of Chemistry, National Institute of Dental Research.

Dr. Edward N. Brandt, Jr., HHS Assistant Secretary for Health, presented Dr. Shannon with a painting of the newly renamed Shannon Building. Following this ceremony, a reception was held at which Dr. Brandt assisted Dr. Shannon in cutting a ribbon around a large framed blowup of the building.

HHS Secretary Richard S. Schweiker, who was scheduled to participate, was unable to attend due to a called Cabinet meeting.

The official portrait and bust of Dr. Shannon will remain in the lobby, in addition to his name cast in bronze on the front of the building.

Bldg. 3 Alumni Gather

Earlier in the day, a coffee was held for Dr. Shannon and former Bldg. 3 alumni who worked there under him during the time he established the intramural program of the then National Heart Institute, an assignment given him by Surgeon General Scheele.

Among the alumni were Dr. Wyngaarden, Dr. Fredrickson, Dr. Axelrod, Dr. Anfinsen, and Dr. Jack Orloff, director, Division of Intramural Research, NHLBI. Also attending were present researchers in Bldg. 3.

Dr. Shannon then visited his old office to meet with Dr. Wyngaarden and key OD staff during which he again sampled his old chair and reminisced about his years as Director and the intricacies involved in establishing the NIH intramural program. A special luncheon in Stone House followed.

One particular anecdote Dr. Wyngaarden shared with the audience during his welcoming remarks provided a graphic example of the differences in personnel practices then and now.

Surgeon General Scheele approached Dr. Shannon asking if he would like to head NIH. Responding affirmatively, Dr. Shannon asked when. To which Dr. Scheele replied “How about Monday!” And it was done.
Six New Members Appointed to 4-Year Terms on NIADDK Advisory Council

Six new members have been appointed to 4-year terms on the National Arthritis, Diabetes, and Digestive and Kidney Diseases Advisory Council. The new members are Drs. Frank P. Brooks, Reginald R. Cooper, Oscar B. Crofford, Carl W. Gottschalk, Frank Hinman, Jr., and John T. Potts.

As council members, they will advise and make recommendations to the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases concerning its program of grants and awards for biomedical research.

Dr. Brooks, an authority on the cause, treatment and prevention of digestive diseases, is presently a professor of medicine and physiology at the University of Pennsylvania School of Medicine. He received his M.D. degree from the University of Pennsylvania in 1943 and an Sc.D. degree from the university in 1951.

He is currently a consultant on gastrointestinal drugs, Food and Drug Administration, a former president of the American Gastroenterological Association, and a founder and president of the Pancreatic Association. He is currently editor of Digestive Diseases and Sciences and former chairman, editorial board, Viewpoints on Digestive Diseases.

Dr. Cooper, a national leader in orthopedic research, is chairman of the department of orthopedics, University of Iowa College of Medicine, and chief of the rehabilitation medical service, Veterans Administration Hospital, Iowa City, Iowa.

He received his M.D. degree from the Medical College of Virginia, his orthopedic surgical training at the University of Iowa, and a research fellowship at Johns Hopkins University.

He is the secretary of the American Academy of Orthopaedic Surgeons, and a former president of the Orthopaedic Research Society. His area of expertise is the biology and ultrastructure of bone in normal and disease states.

Dr. Crofford, a leader in the field of diabetes and endocrinology, is the director of the diabetes research and training center at Vanderbilt University and a professor of medicine at the School of Medicine. He also holds the Addison B. Scoville, Jr., chair for diabetes and metabolism, and has been an associate professor of physiology since 1970.

He received his M.D. degree from Vanderbilt University in 1955. He is past president of the American Diabetes Association and served as chairman, National Commission on Diabetes, from 1975 to 1976.

Dr. Gottschalk, an authority in the physiology, causes, treatment and prevention of kidney diseases, is a career investigator of the American Heart Association and Kenan professor of medicine and physiology at the University of North Carolina.

He received his M.D. degree from the University of Virginia in 1945, and was chairman of the special committee on kidney disease, Bureau of the Budget, from 1966 to 1967.

In 1969, he chaired the biological and medical sciences advisory committee, National Science Foundation, and the NIADDK study that produced the publication, Research Needs in Nephrology and Urology. He is also a member of the National Academy of Sciences.

Dr. Hinman, a noted urologist, is clinical professor of urology at the University of California School of Medicine at San Francisco, and chief of urology at Children's Hospital, San Francisco.

Since 1965, he has been chairman of the School of Medicine's research evaluation and allocation committee. He received his M.D. degree from John Hopkins Medical School in 1941.

From 1970 to 1975, Dr. Hinman served as chairman of the research committee, American Urological Association, and has served as a trustee of the American Board of Urology since 1979. He is a member of the editorial board of Archives of Surgery and International Abstracts of Surgery and has authored over 200 publications.

Dr. Potts, an endocrinologist, is the founder and president of clinical medicine at Harvard Medical School, and chief of general medical services at Massachusetts General Hospital in Boston. He was chief of the endocrine unit there from 1968 to 1981.

He received his M.D. degree from the University of Pennsylvania in 1957, and was a member of the NIH task force on endocrinology and metabolism from 1978 to 1979.

ALKYLATING AGENTS

(Continued from Page 1)

Ten of the ANL patients received melphalan and two received chlorambucil. No case of ANL occurred among those who did not receive alkylating agents. The leukemias developed from 2 to 7 years after treatment.

The findings do not suggest that patients treated with these drugs, or that physicians who use them, should stop or avoid their use, especially for treatment of advanced ovarian cancer. The benefits of these two drugs in the treatment of advanced ovarian cancer are well documented, and these benefits outweigh the risk for ANL.

However, the findings suggest caution in using these drugs in two circumstances: (1) for treatment of cancer patients at low risk of relapse, and (2) for patients with noncancerous conditions when long-term survival and therapy are expected.

For these two types of patients, the NCI investigators strongly recommend that dose and duration of use of the drugs should be kept to a minimum. All cases of ANL in this survey occurred among women who received high doses of the drugs, but it is possible that for effective chemotherapy there may be no absolute risk-free dose level.

The study is part of an ongoing assessment by NCI in collaboration with cancer specialists around the country on late treatment effects in cancer patients. These studies report long-term followup of cancer patients receiving effective therapy and experiencing improved survival.

Ovarian cancer patients were selected for this study because the natural course of this type of cancer is not known to predispose patients to development of leukemia later. The study is the first to quantitatively assess the risk for leukemia from melphalan treatments. This information may be useful in conducting other studies which attempt to identify, if possible, a dose level at which there may be less or no risk for ANL, without compromising the effectiveness of therapy. A summary of this study is available from the Office of Cancer Communications, 496-6641.

Two large murals by American artist Irwin Hoffman were recently installed at the National Library of Medicine. Representing the artist's concept of medical history, the murals are his personal salute to the great men and women of medicine from early Egypt to modern times. Details from the murals are in the illustrations above. Left, Gilman Frost oversees the taking of the first X-ray in America, and right, Alexander Fleming discovers penicillin.
James Roosevelt Addresses NINCDS Employees' Meeting

James Roosevelt's personal motivation for heading the National Committee for Research in Neurological and Communicative Disorders began when his father, President Franklin D. Roosevelt, contracted polio at the age of 39.

When the doctors finally came to the conclusion that my father would never be able to walk again, he experienced a disappointment that caused him physical pain and emotional distress. "It was a blow to his whole system which took him years to get used to," Mr. Roosevelt told the NINCDS staff assembled in Wilson Hall for the institute's annual all-employees meeting on Jan. 12.

Although President Roosevelt had to let go of his dream to walk again, his oldest son hopes that research conducted and supported by the NINCDS will one day lead to a cure for other paraplegics.

Mr. Roosevelt also said he believes that the committee he now heads will play a role in helping to find better ways to treat paraplegia and other disorders.

The NCR is an organization of voluntary health agencies and professional societies that works to increase public understanding and support of biomedical research on neurological and communicative disorders.

Formed as an ad hoc coalition in 1952, NCR was loosely organized until the late 1970's when, according to Mr. Roosevelt, the affiliates "decided to pull together for the overall effort."

The revitalized organization now has nearly 60 members. A primary goal of the committee is to educate Federal, state, and local government leaders as well as members of Congress about research needs.

"For the first time, the Congress has begun to hear a strong voice which represents millions of people affected by these (neurological and communicative) disorders," said Mr. Roosevelt, stressing the need for this advocacy to be based on factual and up-to-date information.

"We must work closely with you," he told the NINCDS audience, "because without your help we could not properly present the story to the public. They want to know what progress you are making, and whether they are getting a proper return on their money."

As part of its effort to increase public awareness of the need for research on disorders of the brain and nervous system and disorders of hearing, speech, and language, NCR has launched a public relations campaign.

NCR has also enlisted the aid of Joan Collins, Ed Asner, Agnes de Mille and Jennifer Jones Simon, among other celebrities, in spreading the word about the importance of research.

Mr. Roosevelt's own efforts to spread the word began officially in June 1982 when he became president of NCR. But he has been involved in health issues for decades.

He is vice-president of the Eleanor Roosevelt Cancer Foundation, and is a trustee for both the March of Dimes/Birth Defects Foundation and the Roosevelt Warm Springs Foundation.

He served six terms as a U.S. congressman from California, and believes that the contacts he made during those years have proved invaluable.

Mr. Roosevelt's appreciation of research is grounded also in his own experience with a neurological disorder. "I am a person who has Parkinson's disease," he revealed, "and without your work I probably wouldn't be able to stand up before you and talk."

Mr. Roosevelt is enthusiastic about future research on Parkinson's disease, spinal cord injury, hearing loss, and other neurological and communicative disorders.

"I would like to be 25 again," he said. "What has happened in my lifetime is almost unbelievable, and what is going to happen in your and your children's lifetime is even more exciting. Research will unlock so much that future historians will call this the wonder age of mankind."

Another Probable Cause Found for Fasting Hypoglycemia

Sweating, trembling, anxiety, nervousness, weakness, fatigue, and hunger are all symptoms of fasting hypoglycemia, an abnormal reduction in one of the body's essential nutrients—glucose. This potentially life-threatening metabolic state can result from a variety of causes, making diagnosis difficult.

Fasting hypoglycemia, a fall in blood glucose after 6 or more hours, is an extremely rare condition, and is not to be confused with the highly controversial reactive or functional hypoglycemia. In reactive hypoglycemia, blood glucose falls within 2 to 4 hours after a meal. Many people wrongly believe they have hypoglycemia because of the nonspecific symptoms. This situation is further aggravated by a misunderstanding of normal blood glucose fluctuations, and by test results from the customary oral glucose tolerance test (OGTT) which are easily misinterpreted.

Fasting hypoglycemia can be caused by potentially more serious conditions such as tumors, inborn errors of metabolism, and autoimmune endocrine disease.

Dr. Simeon I. Taylor, clinical investigator in the Diabetes Branch, National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases, has studied a novel case which puts forth another probable cause.

In contrast to what is normally expected, Dr. Taylor has found that in certain populations of hypoglycemia patients, particularly those with autoimmune disorders such as thyroiditis and systemic lupus erythematosus (lupus), the causative factor in hypoglycemia may be autoantibodies directed against the insulin receptor.

Insulin is the major fuel-regulating hormone in humans. It is secreted into the blood in response to increased glucose and amino acid concentrations. Insulin causes circulating blood cells to take up the excess glucose, and also allows for glucose storage in liver, skeletal muscle and adipose tissue. It also promotes protein synthesis from amino acids. These actions clear the excess glucose and amino acids from the bloodstream, returning elevated levels to normal.

Insulin Must Bind to Receptor

To become biologically active, insulin must bind to a receptor located on a cell membrane. The insulin antireceptor antibody can also bind to the receptor.

When this occurs, three things may happen: the antibody mimics the activity of insulin; the antibody blocks the binding of insulin to its receptor; or it desensitizes target tissues, such as the blood cells, fat cells, and muscle tissue, to insulin's effects.

In the first instance, the binding of antibody to receptor causes insulin-like effects, or a lowering of blood glucose. In the latter two instances, an insulin resistant state occurs. In insulin resistance, insulin is present, but its effectiveness is decreased, and glucose levels remain elevated.

In many patients with known antireceptor antibodies, insulin resistance is generally the result. In Dr. Tayor's patient the converse was shown. Through a series of specific tests, the patient was shown to have autoantibodies to the insulin receptor. When bound to the insulin receptor, these antibodies mimicked the effects of insulin by lowering blood glucose levels.

This finding is particularly important to the diagnosing physician, because one cause of hypoglycemia, which is difficult to diagnose, is insulinaemia. Insulinaemia is a tumor of the pancreatic beta cells, which produce insulin. The treatment for this is surgery. By examining patients for antireceptor antibodies, unnecessary surgery may be avoided.

This research also stimulates additional questions, such as what mechanism determines whether the antireceptor antibody will have an insulin-mimicking or insulin-blocking effect. Further investigation of the problem may provide important insight into the mechanism of insulin action, as well as the cause of insulin resistance.

Dr. Taylor and his colleagues reported these findings in the New England Journal of Medicine (vol. 307, issue 23, p. 1422)
NLM Computer Specialist, Dr. Martin M. Epstein, Dies

Dr. Martin M. Epstein, 41, director of the medical computer science research group, Health Professions Applications Branch, Lister Hill National Center for Biomedical Communications, National Library of Medicine, died Jan. 21 of lymphoma, at the U.S. Naval Medical Center, Bethesda.

Dr. Epstein received a B.S. in mathematics from Brooklyn College, City University of New York in 1963, and was sworn into the PHS Commissioned Corps in 1964. From 1964 through 1980 he was involved in medical computer science research group, and in 1973 from the University of Maryland. He remained un until 1980.

He received an M.S. in computer science in 1973 from the University of Maryland. From 1974 to 1977, he studied at the University of California in San Francisco and Berkeley, spending 2 years as a visiting scientist at SRI International in Menlo Park.

Dr. Epstein returned to NIH as a computer scientist, Office of the Director, DCTR, in 1978. He was granted a Ph.D. in medical information science in 1980 by the University of California, San Francisco. In the same year, he came to the Lister Hill National Center for Biomedical Communications, and was director of the medical computer science research group. His research area had been the application of artificial intelligence to natural language access to clinical data bases. His work at LHNBC was extending this approach to knowledge-based systems derived from the medical literature.

He is survived by his wife, Joyce; his mother, Mrs. Golda Epstein; and a brother, Samuel, both of Morristown, N.J. A memorial service was held at the Main Chapel, National Naval Med. Center Jan. 30. A memorial fund is being established by friends. Expressions of sympathy may be sent to Frances Penenburgh or Susanne Humphrey, Lister Hill Center, Rm. 7E702, Bethesda, MD 20209.

Drs. Grady and Freese Appointed To NIH Library Advisory Committee

Drs. Cheryl L. Grady of the Laboratory of Neurosciences, NIA, and Dr. Elizabeth G.M. Freese of the Laboratory of Molecular Biology, NICHD, have been appointed to the NIH Library Advisory Committee as representatives of their respective Institutes.

They replace NIA member Dr. Joseph Rifkind, who has completed a 3-year membership term, and NICHD member Dr. Eberhard G. Trams, who died in March 1982. The 19-member committee meets four times each year to advise the Director, DRS, and the chief of the DRS Library Branch on library operations.

Much of the committee’s work is done through subcommittees dealing with specific aspects of library operations such as journal retention and computerized bibliographic services.

A list of the current NIH Library Advisory Committee members and their locations follows. They may be contacted on questions and suggestions regarding library policies and operations.

Findings Noted

Findings from this study are consistent with previous studies on larger populations of physically active men: exercise raises the level of HDL2 in the blood and individuals who exercise regularly and vigorously are able to break down fat from plasma more efficiently than those with lower HDL2 levels.

Results of this study suggest that men should stay physically very active since the protective benefits of HDL2 disappear quickly should exercise stop.

Nearly 10 years ago, Dr. Patsch developed the technique for separating HDL2 and HDL3. Using this method, he was able to demonstrate how HDL2 is formed: fat-rich lipoproteins (VLDL) which appear in the bloodstream quickly should exercise stop.

The breakdown empties the particles' cargo of fat, leaving lipoprotein shells that combine with HDL3 to form HDL2-like particles.

He is research associate professor of medicine at Baylor College of Medicine in Houston, Tex. □

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The NIH Record

February 1, 1983
Clinical Center Plans Additional Renovations Starting in February

Starting in mid-February the Clinical Center will begin renovations to provide "areas of refuge" to protect patients in the event of fire.

According to the plan, construction will involve all hospital floors and work should be completed by November 1983. Work will also proceed to convert Bldg. 10 passenger elevators to an automated, rather than operator-controlled, system to enhance efficiency.

Although these operations will cause temporary inconveniences, construction is phased to minimize disruption as much as possible and complete the work as quickly as possible.

Patients endangered by fire must be moved quickly to an area of protection on their floor that meets specific safety criteria. To meet safety regulations, the Clinical Center will upgrade existing areas of refuge and construct new ones to increase exit capacity and decrease travel distance required to move patients to safety.

Plans have been developed to construct areas of refuge on each floor of Bldg. 10 from the roof to the B-1 level. These will be located at the central elevator lobby, the corridors adjoining Bldg. 10 to the ACRF, and in the west wing (D corridor) of Bldg. 10.

Phase 1 of the renovations will begin with the center lobby of floors B-1, 1, 2, 7, 8, 9, and 14, and the west wing of floors 3, 4, and 5. Construction activity on the floors will necessitate closing off certain access routes between the corridors and between Bldg. 10 and the ACRF.

Furthermore, construction requirements dictate that work in the center lobby will close some access routes in the morning and afternoon and different ones in the evening. To correspond with the construction schedule, the center bank elevators will be closed off on the affected floors. The remaining two will operate as usual.

Before any work begins—and as the work progresses—detailed information will be given all involved about what changes will occur, how they will affect patients, staff, and visitors, and what accommodations will be made to compensate for the disruption to routine practices. Signs will be put up to direct traffic flow.

Work will be scheduled in three phases, each involving different floors in the lobby area and the west wing, and each phase will last approximately 11 weeks.

Because traffic in the CC has grown greatly over the years, the elevator service has not been able to keep pace with the demands of patients, staff, and visitors.

A study of the problems and a survey of elevator systems in other hospitals have led to plans to automate passenger elevators to enhance efficiency.

Service of operator-controlled elevators is interrupted several times each day for emergency or other special calls. To alleviate problems these delays cause, the center bank of elevators and the passenger elevators in the B and D wings will be converted to fully automatic service. One elevator each in the B and D wings will be designated for special patient transportation from 7:30 a.m. to 4 p.m. Monday through Friday and will remain operator-controlled to respond to these calls.

Dr. Heidelberger, Noted Cancer Researcher, Dies

Dr. Charles Heidelberger, 62, an internationally recognized cancer scientist, died of cancer Jan. 18.

Dr. Heidelberger was a pioneer in the development of drugs called antimetabolites for the treatment of cancer. These drugs are designed to be similar to components that cells need to reproduce and survive.

During the 1950's, he noticed that some rapidly developing cancers were using a disproportionate amount of a metabolite called uracil, an essential building block for cell division.

He changed the molecular composition of this natural metabolite by introducing a fluorine atom into its structure. The resulting antimetabolite, 5-fluorouracil, is so similar to the size and shape of uracil that the cancer cell is tricked into using it. The 5-fluorouracil blocks an essential metabolic pathway and leads to the death of the cell. Today, 5-fluorouracil is still a standard component of treatment programs for several cancers.

"His contributions to cancer research were pioneering and illuminated the fields of cancer chemotherapy and chemical carcinogenesis. His death is a great loss to the National Cancer Program," said Dr. Vincent T. DeVita, Jr., NCI Director.

Dr. Heidelberger spent 27 years on the oncology faculty of the University of Wisconsin McArdle Laboratory for Cancer Research. He has been a member of numerous scientific advisory committees, including the board of scientific counselors of NCI's Division of Cancer Treatment.

Whenever people stop thinking for themselves, there is always someone willing to step forward and do their thinking for them.—Hatton W. Summers

Dr. Abner L. Notkins, chief, Laboratory of Oral Medicine, NIDR, was the first recipient of the Paul E. Lacy Research Award in diabetes presented last month in Washington, D.C., during the first national conference on Utilization of Human Tissues. Co-recipient of the award was Dr. Freda Ginsberg-Feliner of Mt. Sinai Hospital, N.Y., who collaborated with Dr. Notkins. Each received a microscope sculptured in transparent acrylic by Aviva Pussow of Philadelphia and a $2,500 cash award. The recipients were cited for their work on the role of hereditary and environmental factors in the development of insulin-dependent diabetes.
Diagnosis, Treatment, and Research of Lung Cancer Discussed During Layman Lecture

Dr. John Minna, chief of the NCI-Navy Medical Oncology Branch, discussed lung cancer in the final 1982 Medicine for the Layman lecture. He stated at the outset: "If I have one message to leave with the audience tonight—particularly the younger members—it is, 'Don't smoke.'"

Although lung cancer may result from exposure to toxic agents such as asbestos, radiation, and certain metals and chemicals, the major risk factor by far is tobacco smoke. One in 12 heavy smokers develops the disease. Whereas the death rates for most other forms of cancer are on the downturn, mortality from lung cancer is steadily rising. In 1980, there were 107,000 new cases of lung cancer, and most of these patients died within a year of diagnosis.

Only 10 percent of lung cancers are detected through early screening methods such as X-rays or sputum examination. Because lung cancer cells grow so rapidly, the vast majority of cases are not discovered until the patient develops symptoms. Lung cancer cells first arise in the bronchi, where they cause hoarseness, pain, cough, difficulty breathing and swallowing, and irregular heartbeats. If the tumor has spread (metastasized) to other parts of the body, additional symptoms will appear.

Metastasis to the brain, bone, or liver can cause headache, weakness, bone fractures, jaundice, bleeding, and pain, depending on the organs affected. Lung cancer cells can also produce hormones that affect other body systems, causing a "paraneoplastic syndrome." For example, the cells may produce a hormone, arginine vasopressin, which acts on the kidneys to decrease sodium concentration in the body. This in turn can cause severe confusion and even coma.

Once lung cancer is suspected or confirmed, a series of diagnostic tests is done to determine the location and extent of the tumor, and the probability of achieving a cure. A tissue biopsy is done to determine whether the tumor cells are indeed malignant and, if so, whether they are one of the types classified as "non-small cell" or if they are "small cell" lung cancer. This information will influence the treatment.

A careful history and physical examination, plus X-ray, radionuclide, and CAT scan studies are done to see if the tumor appears confined to the primary site in the lung or if it has spread to other parts of the body, particularly the brain, bone, and liver.

Localized, non-small cell lung cancers respond best to surgery or radiation therapy, both directed at removing or killing all the cancer cells at the local site. Small cell lung cancer, on the other hand, can almost never be cured by surgery or radiotherapy alone because the tumor spreads so quickly. Therefore, chemotherapy is used to combat both the local and metastatic tumors, while radiotherapy may also be recommended to treat the primary tumor.

Actual cure rates for lung cancers vary. At present, about 10 percent of patients with non-small cell cancer treated surgically are cured, while 5 to 10 percent are cured with radiotherapy; and about 12 percent of small cell lung cancers are cured through chemotherapy.

These are overall cure rates. However, the percentages differ for specific tumor types at specific disease stages.

For patients in whom there is no reasonable chance of cure at the outset, therapy is directed primarily at relieving symptoms—perhaps through radiotherapy or chemotherapy aimed at shrinking the tumor, treating infections and heart problems, prescribing pain medication, and providing emotional and psychological support.

Research at NIH is directed to improving present cure rates, and Dr. Minna is optimistic about the possibilities for the future. "However," he said, "the first goal must be prevention, and the most obvious way to prevent lung cancer is to not smoke."

Even for people who do smoke, the risk of disease decreases immediately upon stopping and continues to drop over the years until it is almost the same as that of people who have never smoked.

Researchers have recently found genetic changes in some lung cancer DNA that may explain what causes cells to become malignant. Besides contributing to our fund of basic knowledge, this discovery may eventually enable physicians to identify smokers genetically predisposed to the disease before it develops.

Meanwhile, research aimed at developing improved therapies for lung cancer is taking off in many new and exciting directions. Scientists have just recently succeeded in growing lung cancer cells outside the body (in vitro) and are testing their sensitivity to various drugs. Early results suggest that the cells respond to these drugs in vitro the same as they do in the body.

If this is so, the therapeutic implications of these advances in basic science and their implications for clinical application: "Although lung cancer is a major health problem only infrequently cured with current treatments, we are gaining new insights in the laboratory that should enable us to attack this problem with new and better tools."
DR. GUROFF
(Continued from Page 1)

chief of the section on intermediary metabolism in NICHD's Laboratory of Developmental Neurobiology.

The author of more than 120 scientific papers, Dr. Guroff edits an annual series of volumes entitled *Growth and Maturation Factors* and wrote the text, *Molecular Neurobiology*.

His research interests include amino acid metabolism in the brain, mechanisms of hydroxylation, and animal models of mental retardation. He participated in the discovery of the hydroxylation-induced migrations, now known as the "NIH shift."

Dr. Guroff's recent work has been focused on understanding the mechanism of action of nerve growth factor. He plans to remain active in the research laboratory while serving in his new position.

He is a member of several scientific societies, including the American Society of Biological Chemists, the International Society for Neurochemistry, and the Society for Neuroscience.

Cross-Country Skiing Planned

R&W will sponsor a cross-country skiing trip on Saturday, Feb. 12. The Outdoor School, Inc., will use the closest facility available that has snow. They will travel no farther than New Germany State Park in western Maryland.

The trip is for beginners and intermediate level skiers. Well-qualified instructors will help ensure an enjoyable day on the snow.

Cost is $26.75 per person. Sign up at the R&W Activities Desk, Bldg. 31, Rm. 1A18.

ARMAND HAMMER
(Continued from Page 1)

patient is still in a complete remission 1½ years since receiving experimental therapy.

Dr. Levy has received a number of academic honors and awards and has written extensively in his major research interest areas of immunology, cancer biology and medical oncology.

He is currently serving as associate professor of medicine in the division of oncology at Stanford Medical School.

![Dr. Levy](image)

Dr. Levy graduated from Harvard University and received his M.D. degree from Stanford in 1968.

Ultrasound Shown as Possible Diagnostic Tool

Stanford University scientists have demonstrated a new use for ultrasound—to detect blood clots in the vessels of critically ill infants monitored by umbilical artery catheters.

The use of noninvasive ultrasound, they hope, will spare newborns from the potentially negative effects of radiation, while providing doctors with a quick and safe screening method for a variety of catheter-associated complications.

In the past, these babies have been subjected to the use of angiography, a method which provides doctors with X-ray visualization of blood vessels following the introduction of contrast material.

Dr. David Oppenheimer and colleagues, in research supported in part by a grant from the General Clinical Research Centers program of the Division of Research Resources, have found that sonography—previously used effectively to locate umbilical artery catheters—is equally suited for detecting thromboses, or clot formation, in the aorta and nearby arteries.

In a paper presented to the annual assembly of the Radiological Society of North America, Dr. Oppenheimer explained, "Sono-grams can be performed at cribside without removing infants from the intensive care environment. Diagnostic information is obtained without associated ionizing radiation and iodinated contrast material."

In a clinical study at Stanford, 71 neonates with umbilical artery catheters received a series of ultrasound exams. All echoes not representing the catheters themselves were considered indicative of an abnormality. (Normal vessels, Dr. Oppenheimer said, are free of these types of echoes.)

In one instance the catheter itself, by completely filling an inner blood vessel, appeared to obstruct normal blood flow.

This caused ischemia, or blood deficiency in the area, and pulsations were absent. When the catheter was withdrawn, pulsations returned.

Dr. Oppenheimer explained that umbilical artery catheters are never used unless absolutely necessary in patient treatment, but that without them "many more babies would die." The umbilical artery provides the easiest route for monitoring the movements and forces involved in blood circulation.

In his study he found ultrasonically detected abnormalities persisted from 2 to more than 70 days. Many lasted long after clinical symptoms had resolved. In one baby, Dr. Oppenheimer said, the abnormality was mobile rather than fixed to the vascular wall.

This moving "flap," he said, may have been causing the patient's hypertension. He hypothesized that the flap represented either a floating clot or a layer of vessel wall which had torn off during catheter insertion.

"This type of abnormality has not previously been demonstrated in a catheterized infant," he added. "Our ultrasound exams led us to detect it." Moreover, in a variety of cases ultrasound was able to identify clots and other obstructions causing ischemic symptoms in the babies.

Further work, Dr. Oppenheimer said, is required to determine the long-term prognostic significance of ultrasonically detected vascular abnormalities and the impact of their detection on patient care.

He has demonstrated, however, that ultrasound can be useful as a diagnostic tool in catheterized infants. "It is likely that future diagnostic techniques will provide even more accurate analysis of flow limiting lesions," he concluded.

The report was coauthored by Drs. Barbara Carroll and Karen Garth of the division of diagnostic radiology, and appeared in the December 1982 *Radiology*. 

The NIH Record
Dr. S.M. Schwartz Retires; DRG Associate Director

Some 400 friends and colleagues attended a reception on Jan. 7 in the Westwood Bldg. to honor Dr. Samuel M. Schwartz on his retirement from Federal service.

At the time of his retirement, Dr. Schwartz was associate director for scientific review and chief of the Scientific Review Branch in the Division of Research Grants. He provided policy direction and coordination for the referral and initial scientific merit review of grant applications requesting research support from the PHS, and was also responsible for the management of approximately 85 study sections.

He received his B.Sc. degree from the University of Manitoba, Winnipeg, Canada, in 1952 and his Ph.D. degree from the University of Minnesota in 1956. Afterwards, he joined the staff of George Washington University as an assistant professor, progressing to associate professor in 1960.

Dr. Schwartz joined NIH in 1964 as a health scientist administrator in the National Cancer Institute's Research Grants Branch. He later transferred to DRG as executive secretary of the medicinal chemistry "A" study section. In 1968, he became assistant chief for referral.

He left DRG in 1971 to become deputy associate director of the extramural and collaborative programs, and chief of the Scientific Programs Branch, National Eye Institute. In 1973, he became associate director for review and chief of the Review Branch, National Heart, Lung, and Blood Institute. He returned to DRG in 1979 as associate director.

During his 18-year tenure with NIH, Dr. Schwartz helped direct the scientific and administrative management of the extramural programs and was involved in all aspects of the initial scientific merit review process associated with the programs.

Women Volunteers Wanted for Tests

The Uniformed Services University of the Health Sciences needs women volunteers as subjects in an exercise stress test. For further information, call Sue Wigutow at 295-3523.

Elizabeth Shelton, Former Patient, Now Donates Regularly to CC Blood Bank

Elizabeth Shelton, secretary to the NIH Associate Director for Program Planning and Evaluation gives blood at the Clinical Center Blood Bank because, she said, "I know it's needed."

One important reason she now works at NIH and can give blood regularly, is that she was diagnosed and treated successfully years ago at the Clinical Center for a condition that had stumped a number of doctors. When Ms. Shelton was 18 and in school in Northampton, Mass., she became aware of an unexplained fatigue and weakness that lingered during the summer without getting better or worse. She chalked it up to the slow summer and homesickness, and by fall it was better.

Four years later, she began to have episodes once a year in which one eye became inflamed. Each time the inflammation occurred, that eye would be blinded for a month. Over the years of recurrences, she was becoming peripherally blind.

A number of doctors failed to diagnose the condition. After 4 years of recurrences and fruitless examinations, she went to a doctor who, she found, was a consultant for the then National Institute of Neurological Diseases and Blindness. He referred her to the Clinical Center, a hospital no more than a year old at the time.

After 4 or 5 days of tests, the examining physicians suspected toxoplasmosis, a condition caused by an infection by a one-celled organism. Generally such infections in adults cause only mild symptoms, if any. In unusual cases, like Ms. Shelton's, they can cause more serious problems, among them chronic eye inflammation.

The NINDB doctors prescribed an oral drug specific for the organism that causes toxoplasmosis. Following that treatment, Ms. Shelton has never had a recurrence of her symptoms.

When she came to NIH as a patient, she was working full-time at the World Bank and going to school at night. When her first son was born, she remained at home to raise him and later, two more sons. None of the children was affected by the infection.

As soon as physicians were confident that her now cured condition was not a contraindication to her giving blood, Ms. Shelton began regular donations of both blood and blood components such as platelets and white cells.

"Whenever they call, I'm willing to go," she said, even for the longer procedures in which blood components are collected. "Everyone is so pleasant," she said of Blood Bank employees. "They are extremely solicitous of your welfare."

Donors like Ms. Shelton are essential to provide the blood needed for research at NIH. But more are needed.

Of some 13,000 employees at NIH, only 2,084 supply 66 percent of the blood needs for the Clinical Center. Call 496-4508 if you would like to donate.

Ms. Shelton has been working at NIH for the past 17 years.

Five NHLBI employees received NIH Merit Awards in a recent ceremony. Dr. Claude Lenfant (l), NHLBI Director, is shown after the presentations with four recipients (l to r): Eleanor C. Bruckwitz, Division of Intramural Research; Loretta J. Allion, Division of Blood Diseases and Resources; Dr. Carol E. Vreim, Division of Lung Diseases; and Ellis Mullinix, Office of the Director. Leslie L. Jenkins, Division of Intramural Research, was not present.
Dr. McMillan Honored by Heart Association

Dr. Gardner C. McMillan, associate director of the arteriosclerosis, hypertension and lipid metabolism program, Division of Heart and Vascular Diseases, NHLBI, was one of three recipients of the American Heart Association Scientific Councils' Distinguished Achievement Award at AHA's annual scientific sessions meeting held recently in Dallas.

The award recognizes significant contributions to scientific knowledge in cardiovascular medicine and to the affairs of the American Heart Association or one of its 14 scientific councils.

Dr. McMillan joined the (then) National Heart Institute in 1968 as visiting scientist and special assistant to the director. From 1969-1972, he served as visiting scientist and chief, Arteriosclerotic Diseases Branch, Extramural Research and Training, NHLI.

In 1972, Dr. McMillan assumed the duties of associate director for etiology of arteriosclerosis and hypertension, Division of Heart and Vascular Diseases. He assumed his present duties in 1979.

Before joining NIH, he resided in Canada and was heavily involved in arteriosclerosis research at McGill University. While at McGill, he studied the effects of amino acid deficiency on experimental arteriosclerosis. He was one of the first to become interested in the possible use of trans-fatty acids on experimental arteriosclerosis. He also used radioautographic methods to study DNA synthesis in the cells of arteriosclerotic lesions.

Dr. McMillan has served on the research committee of the American Heart Association as vice-chairman and chairman.

Dr. McMillan has served on numerous committees of the council on arteriosclerosis and was chairman of its program committee, vice chairman of the council, and later, chairman.

Dr. McMillan, through his work at NICH, emphasizes research to identify infants at risk for mental retardation and develop strategies to lessen the deficits of retardation.

Visiting Scientists Program Participants

Sponsored by Fogarty International Center
11/8 Dr. Dan Zilberstein, Israel, Laboratory of Parasitic Diseases. Sponsor: Dr. Dennis Dwyer, NIAID, Bldg. 5, Rm. 205.
11/12 Dr. Mauricio Bitulco, Italy, Laboratory of Biochemical Pharmacology. Sponsor: Dr. Leonard Kohn, NIHDD, Bldg. 4, Rm. B1-31.
11/12 Dr. Paul Clarke, United Kingdom, Biological Psychiatry Branch. Sponsor: Dr. Agu Pert, NIMH, Bldg. 9, Rm. 1NN11.
11/14 Dr. Periakaruppan Manoharan, India, Laboratory of Cellular and Molecular Aging. Sponsor: Dr. Joseph Rikkind, NIA, CRC, Baltimore, Md.
11/14 Dr. Siddhardha Roy, India, Laboratory of Chemical Biology. Sponsor: Dr. Hiroshi Tanuchi, NIHDD, Bldg. 10, Rm. 9N260.
11/17 Dr. Hsu Pingshuan, China, Laboratory of Neuropsychology. Sponsor: Dr. Mortimer Mishkin, NIMH, Bldg. 9, 1N107.
11/17 Dr. Renu Bansal Lal, India, Laboratory of Microbial Immunity. Sponsor: Dr. Thomas Chudley, NIAID, Bldg. 5, Rm. 22B.
11/18 Dr. Giuseppe Bruno, Italy, Experimental Therapeutics Branch. Sponsor: Dr. Thomas N. Chase, NINRCS, Bldg. 10, Rm. 5N219.
11/19 Dr. Hisanaga Igarashi, Japan, Laboratory of Cellular and Molecular Biology. Sponsor: Dr. Stuart Aaronson, NCI, Bldg. 37, Rm. 1A07.
11/22 Dr. Neil Gibson, United Kingdom, Laboratory of Molecular Pharmacology. Sponsor: Dr. Kurt Kohn, NCI, Bldg. 37, Rm. 5O19.
11/22 Dr. Jun-ichi Kira, Japan, Laboratory of Cerebral Metabolism. Sponsor: Dr. Marlan Kies, NIMH, Bldg. 36, Rm. 1A27.
11/22 Dr. Shao Zuo-hua, China, Laboratory of Preclinical Studies. Sponsor: Dr. Forrest Weight, NIAAA, Danac, Rm. 5.
11/22 Dr. Takashi Yagi, Japan, Laboratory of Molecular Carcinogenesis. Sponsor: Dr. Rufus Day, NCI, Bldg. 37, Rm. SC25.
11/22 Dr. Xu Young-Hua, China, Laboratory of Molecular Biology. Sponsor: Dr. Jenette Henri, NCI, Bldg. 37, Rm. GB7.
11/23 Dr. Dubo Bojanowski, West Germany, Molecular Disease Branch. Sponsor: Dr. H. Bryan Brewer, NHBLL, Bldg. 10, Rm. 7N117.
11/23 Dr. Masato Ohshima, Japan, Laboratory of Comparative Carcinogenesis. Sponsor: Dr. Jerry Rice, NCI/FCRF, Bldg. 538, Rm. 20A.
11/29 Dr. Devjani Chatterjee, India, Laboratory of Molecular Genetics. Sponsor: Dr. Jacob Maelzel, NICH, Bldg. 6, Rm. B2-27.
11/29 Dr. Jennette Henri, France, Epidemiology and Field Studies Branch. Sponsor: Dr. Peter Bennett, NIHDD, Bldg. 10, Rm. 5O19.
11/29 Dr. Lu Sheng-dong, China, Laboratory of Molecular Biology. Sponsor: Dr. Max Gottesman, NCI, Bldg. 37, Rm. GB7.
11/30 Dr. Than Tam Quach, France, Laboratory of Preclinical Pharmacology. Sponsor: Dr. Erminio Costa, NIMH, Wm. A. White Bldg., St. Elizabeths Hospital.
11/30 Dr. Hiroaki Takashima, Japan, Laboratory of Cell Biology. Sponsor: Dr. Ettore Appella, NCI, Bldg. 8, Rm. 250.
12/1 Dr. Wieslaw Gessner, Poland, Laboratory of Chemistry. Sponsor: Dr. Arnold Brossi, NIHDD, Bldg. 4, Rm. 135.
12/1 Dr. Donata Rimoldi, Italy, Laboratory of Cellular Carcinogenesis and Tumor Promotion. Sponsor: Dr. Luigi M. Deluca, NCI, Bldg. 37, Rm. 2B26.
12/1 Dr. Joseph Rosenoir, Sierra Leone, Laboratory of Pharmacology. Sponsor: Dr. M. W. Alexander, NIHDD, Bldg. 9, Rm. 1M27.
12/1 Dr. Sarah Sariban-Sohrabry, Belgium, Laboratory of Kidney and Electrolyte Metabolism. Sponsor: Dr. Joseph Handler, NHLBI, Bldg. 10, Rm. 6N315.

Three NIEHS Scientists Honored for Biometry Paper

Three scientists from the National Institute of Environmental Health Sciences have been awarded the George W. Snedecor Memorial Award for the best publication in biometry for 1981 by the American Statistical Association, headquartered in Washington, D.C.

Drs. Barry H. Margolin and Norman Kaplan, both of the biometry and risk assessment program, and Dr. Errol Zeiger of the toxicology research and testing program coauthored the paper, Statistical Analysis of the Ames Salmonella/Microsome Test, which appeared in the June 1981 Proceedings of the National Academy of Sciences.

The paper applied statistical principles to the analysis and interpretation of a widely used short-term test which screens chemicals to see if they cause mutation. The Ames test, as it is called, used bacterial cultures which react when exposed to chemicals with mutagenic properties.

Advantages are that it is more rapid and less expensive than other toxicological tests using laboratory animals such as rodents.

February 1, 1983
The NIH Record Page 11
NIH Observes Birthday of Martin Luther King

On Jan. 12, NIH celebrated the birthday of the late Dr. Martin Luther King, Jr. The keynote speaker, Dr. Samuel Proctor, told the audience that Dr. King was the right man, at the right place, at the right time. He said that it is so providential for someone to be ready to serve mankind.

Dr. King had a careful use of language, and always had control of his ideas. He was capable of keeping a commitment, Dr. Proctor said. He was unmov ed by the harassment of those who opposed his ideals.

Dr. Proctor also said that Dr. King brought discipline and information to mankind. He mentioned the Rosa Parks' experience on the bus in Montgome ry, Ala., that triggered the black revolution in the South, and this experience had an impact on the progress of blacks as well as how symbolic Rosa's stand for racial equality was in keeping with the nonviolent philosophy of Dr. King.

The young people should discipline themselves to the sciences and technologies, Dr. Proctor said.

—Jasper Cummings

Dr. Milo D. Leavitt, Former NIA Official, Dies

Dr. Milo David Leavitt, Jr., died of cancer on Jan. 12.

Dr. Leavitt had served as special assistant to the director of the National Institute on Aging as well as deputy associate director of the Institute's Biomedical Research and Clinical Medicine Program from 1978.

One of his responsibilities was the development and direction of the NIA Geriatric Medicine Academic Awards Program to encourage medical schools to improve their curricula with the goal of better medical treatment of the elderly.

Dr. Leavitt had a long and illustrious career of public service. From 1968 to 1978, he served as Director of NIH's John E. Fogarty International Center for Advanced Study in the Health Sciences, and was a member of the U.S. Delegation to the 25th, 26th, 27th, and 28th World Health Assemblies in Geneva, Switzerland.

He held a number of key positions at NIH and also served as science policy coordinator, and deputy assistant secretary for science and population of the Department of Health, Education and Welfare (now Department of Health and Human Services).

Born on June 24, 1915, in Beloit, Wis., and educated at the University of Wisconsin, Dr. Leavitt studied medicine at the University of Pennsylvania and received his M.D. in 1940. He received an M.S. degree in internal medicine from the University of Minnesota in 1948 and an M.P.H. from the School of Public Health at Harvard University in 1959.

He is remembered by his colleagues as a warm, witty, and supportive friend who will be sorely missed.

A Milo David Leavitt, Jr., M.D. memorial lecture fund is being established by staff of the National Institute on Aging. Contributions to this fund may be addressed to Dr. Edward L. Schneider, National Institute on Aging, Bethesda, Maryland 20205.