NIH Has Authority and the Will to Assure Humane Treatment of Animals in Research

But Ultimate Solution Should Be Educative, Not Regulative, Dr. Charles McCarthy Thinks

Biomedical research using animals has been prominent in the news lately, most immediately at NIH because of a recent 4-day sit-in by an animal rights group.

Because many NIH employees may not be familiar with NIH policies on experiments in which animals are used, Record Editor Herschel Cribb interviewed Dr. Charles McCarthy, director of the Office for Protection Against Research Risks, to get an overview of NIH's role in the care and use of animals both in its own laboratories and under projects it funds at other biomedical institutions. Highlights from the interview follow:

Q. Why is it so important that we have animal research? I understand that biomedical science is based largely on the assumption that the results from animal experiments can be transferred in most cases to human beings to explain or heal human diseases. Is that true and what is the evidence for it?

A. Yes, it certainly is true. As a matter of fact, I think the overwhelming majority of significant advances in biomedical science that have been made in the last 50 years have involved prior research with animals. And I think one of the things that may not be well understood is that biomedical research not only benefits human beings—I think everybody knows that—but it also benefits animals. And, therefore, the health of animals is greatly enhanced by this research though that may not be the primary purpose.

Q. Many people ask why can't you substitute computer simulations for a lot of these medical experiments? Why can't you?

A. Well, of course in some cases we can and do, and NIH is putting an enormous amount of effort into finding alternatives to the use of animals. When we use that word "alternatives", we mean that portions of the research can be carried out by computer or by in vitro processes in the laboratory. But I don't think anyone at present foresees a time when the effect of a new device, a new drug, a new procedure will not have to be tried—not just on a computer or in the laboratory—but on a living organism. These organisms are so complex that one cannot ever anticipate all the effects of a new procedure and crank that into a computer model or into a laboratory test. It is true that because of computer modelling and in vitro processes, the numbers of animals used in research have been decreasing each year and we think that's...
Daycare, Summer Camp Available to NIH Children

The Preschool/School-Age Program, providing group care for children ages 3 to 12, operates at the Aylawn Center near NIH. Open 5 days a week, Monday through Friday from 7:30 a.m. to 6 p.m., the program provides full-time care for preschoolers and before and after-school care.

Transportation is provided for children attending Rosemary Hills Primary School, Wyngate, and North Chevy Chase Elementary Schools.

There are full day programs during school holidays and winter and spring vacations. The Aylawn program has a diversified staff of teachers and teacher aides.

Summer Care
POPI, Inc. also provides summer care for preschoolers and school-age children at Aylawn.

There are five 2-week sessions during the summer months. Activities include Spanish speaking lessons, sign language, swimming (three times a week), gymnastics, aerobics, drawing, drama, and crafts. Field trips are also included. Recently the children visited The Smithsonian Institution's American History Building.

Further questions on the Aylawn program may be directed to Anne Schmitz, 530-5550,—Marilyn Berman

Women Runners, Non-Runners Needed as Volunteers For Hormone Study

Volunteers are needed for a study on hormonal changes in female long distance runners. Two categories of women will be tested:

• women running 35 or more miles per week, and
• women doing little or no exercise.

Women volunteers must be between 18 and 40 years old, be non-smokers, not taking any medications that would affect their hormone levels.

Each subject will come to the lab for two or three sessions. As part of the study, volunteers will receive a maximum EKG treadmill test, body fat determination by both skinfold and hydrostatic weighing methods, and then individual hormone levels determined by taking blood samples.

If you are interested in participating in this study, call Janet Yu-Yahiro, Department of Physiology, Uniformed Services University, at 295-3623 or 295-3511.

Normal Volunteer Program Wants To Contact Former NIH Volunteers

The Normal Volunteer Program is interested in knowing how many former college student normal volunteers are now, or have been, employed at NIH following their normal volunteer experience as students.

Former volunteers who are now working at NIH and researchers who have had former normal volunteers employed in their laboratories are asked to contact Loretta Coughlin, assistant chief. Normal Volunteer Program, 496-4763.
New Test Has Screened-Out AIDS Contaminants
From Nation's Blood Supply, Expert Conferees Say

A new test licensed last spring has apparently succeeded in screening out AIDS-related contaminants from the Nation's blood supply used for transfusions. These blood sample studies were reported on July 31 at a meeting cosponsored by NIH, the Food and Drug Administration, and the Centers for Disease Control.

The blood tests are doing an extremely good job of screening the general population and are extremely valuable in screening out infectious blood contamination with the virus that causes acquired immune deficiency syndrome, according to Dr. Harry M. Meyer, director, Center for Drugs and Biologics, Food and Drug Administration.

The conference spokesmen said they believe that virtually all donors with suspect blood are being identified and their blood eliminated from the system.

The results of the test were based on more than a million units of blood collected from 131 centers in the U.S. from April 22 to June 16, 1985, representing about 70 percent of the blood collected at those centers.

Transfusion-associated AIDS accounted for about 2 percent (202 cases) of the 12,067 AIDS cases reported to the CDC through July 26. Of the overall total, 6,079 cases have been fatal thus far.

The test measures the amount of antibody that the body produces in response to the presence of HTLV-I, the virus that is believed to 'cause' AIDS. The test does not detect the virus itself but a close correlation was found in one study between presence of the antibody and a later discovery of the presence of the virus.

Three variants of the blood test were reported. These are produced by Abbott Laboratories, Electronucleons and Litton Industries. The tests are derived from one developed last year by Dr. Robert Gaillo's team at the National Cancer Institute.

Despite the advance made by the new blood test, the number of transfusion-associated AIDS cases will continue to rise, but probably at a steadily decreasing rate, said Dr. James W. Curran, chief, AIDS Branch, Division of Viral Diseases, CDC. That is because the incubation period of the disease is so long—up to 6 or 7 years—and the disease can affect those who received transfusions before the blood tests were introduced.

Dr. Curran also said that transfusion-associated AIDS had been reported in 33 states. He said he thought that compliance with recommendations by high-risk groups to refrain from donating blood may have done as much, if not more, than the test to protect the blood supply from AIDS.

Of the 202 transfusion-associated AIDS cases, 82 cases were contracted by hemophiliacs who probably got the disease through the blood plasma product called Factor VIII, a clotting agent. In addition to identifying suspect donor blood, Factor VIII is receiving double protection from AIDS contamination. First it is examined through the antibody test and then a heat-treatment procedure is used in manufacturing the plasma products, which is still being evaluated in these blood products.—Joyce McCarthy

Retirement Deposit For Military Service

In November 1983, NIH employees were notified of procedures to be followed for making a pension deposit for post-1956 Military Service and were advised that the deposit must be made prior to retirement.

Employees planning for retirement were advised to hold/invest the amount of the deposit until Oct. 1, 1985 (or retirement if sooner) since deposits were interest free until that date. FPM letter B31-B4, dated June 28, 1985, states that no interest will be charged on deposits made before Sept. 30, 1986.

Employees planning for retirement are, therefore, advised to hold/ invest the amount of deposit until Sept. 29, 1986. After that date, the deposit will be 7 percent of the military basic pay received for such service, plus interest at a variable rate identified by the U.S. Treasury Department.

Scott Jones, son of Thomas S. Jones, whose medical illustrations are on display in the main lobby of the National Library of Medicine, recently visited NLM to view the exhibit honoring his father. On display until Oct. 1, the exhibit includes many of the famous illustrator's original medical works, examples of books and journals in which his illustrations and educational theories appeared, and a selection of nonmedical paintings never before publicly displayed.
Part-Time DRR Staffer Proves a Computer Whiz

Building a better mousetrap was never one of Eric Greenberg’s goals. But, symbolically speaking, he built one anyway.

In fact, Greenberg’s brainchild—Tablecalc, an innovative software package enabling administrators to better manage and track institutional grants—is so highly regarded that it is being used throughout NIH, not just in the Division of Research Resources where he devised it. It is also being adopted for use by the Departments of Agriculture and Defense, and the Nuclear Regulatory Commission.

Besides conceiving and writing Tablecalc and other computer programs, Greenberg has also been intimately involved in other computer-related activities for the Data Management Section of DRR.

“Eric’s really involved in a lot of projects,” says Ric Shafer, DRR executive officer.

“Tablecalc,” says Shafer, “has provided us—and others outside the division—with a software package which makes it easier to get the computer to do what you want it to do.

“His second major contribution is that he essentially has become the division’s PC (personal computer) expert; he’s helped the staff understand the power and capabilities of PCs, as well as tutored them on how to use various applications. He’s even written a handbook which uses layman’s terms to describe how to operate a PC.”

Greenberg has also helped procure new computer equipment by evaluating and testing different models. He is currently upgrading the division’s report producing information systems using WYLBUR’s command procedures, which greatly reduces the number of commands required.

“And by using this higher level program language, we are able to decrease processing time, thus increase efficiency,” Shafer added.

Because of his accomplishments, the division recently presented Greenberg with a sizeable Special Act or Service Award, a rare achievement for a part-time employee.

Part-time? Yes; part-time.

You see, what’s remarkable about this story is that because Eric attends school fulltime at the University of Maryland in College Park, he only works 10 to 15 hours a week at DRR.

“I’m an EE (electrical engineering) major,” says the 22-year-old honor student, “and I’m going to graduate in December.

Two and one-half years ago when hired as a GS-3 computer clerk, Eric was concerned that the job might not challenge him enough.

“Originally, I was told to sit down at my desk with a ruler and pencil and edit lines of computer programs, correct errors in how programs were written.

“But I couldn’t see wasting my time doing that when I knew there had to be easier ways. So I wrote a computer program to do the editing. From then on, every time Jean (Jean Babb, Eric’s supervisor) gave me something to do, I’d write a program to do it.

“I’ve never been the rebellious type,” he says, “but I knew I could figure out a way to use my mind to make the job easier. I guess I’m better at using my mind than I am at taxing my patience.”

Once the range of Eric’s talents and skills became evident, the complexity of his job ballooned. And he’s happy for the opportunity.

“Not only has the job been great in that the division has been extremely flexible in permitting me to work around my classes, but the job has been beneficial because I can show prospective employers something tangible when I begin interviewing this fall,” Greenberg noted.

A lot of people throughout the division will miss Eric Greenberg when he graduates. “We’ve been fortunate to have him,” says Shafer, “he’s done much more than we ever imagined.”

—Michael Fluharty

Dave Lynch, Crew Win Regatta; Sailing Lessons Start in Sept.

Dave Lynch skippered the 19-ft. Flying Scot Wingit to victory in the first of four NIH Sailing Association (NIHSA) regattas for 1985. His crew, Amy Rosenberg and Karl Arrington.

The NIHSA’s Basic Training Course, including six Wednesday evening classes and three on-the-water sessions, will start Sept. 4. Cost is $75 plus $30 NIHSA dues.

Sign-ups will be Aug. 28 at 9 a.m., Bldg. 31, R&W Activities Desk, where more information on the NIHSA and the Basic Training Course is available.

The NIH Sailing Association’s Wingit sails to victory with skipper Dave Lynch and crew Amy Rosenberg and Karl Arrington.

Dr. Arthur Merrick Retires From NHLBI After 20 Yrs.

Dr. Arthur W. Merrick, chief of Program Projects Review Section, National Heart, Lung and Blood Institute, will retire this week after more than 20 years’ government service.

A native of Great Falls, Mont., Dr. Merrick began his studies at the University of Montana, Missoula, but was interrupted by World War II. His service career began in December 1941 and extended until June 1948. Serving with the 41st Infantry Division Dr. Merrick earned the Silver Star, Bronze Star, Purple Heart with two clusters, Presidential Unit Citation, Combat Infantry Badge and various campaign citations.

He was active in the Army Reserve until 1970, retiring with the rank of Lieutenant Colonel.

Dr. Merrick returned to his education in 1948 at the University of Montana and earned bachelor’s degrees in zoology, in botany and in wildlife technology. He began his graduate studies in Montana but transferred to the University of Missouri, Columbia, where he earned his master’s degree and Ph.D. in physiology.

Dr. Merrick arrived at NIH after having taught at the University of Kansas, the University of Illinois State University. He began as a health scientist administrator in the NHLBI Cardiac Diseases Branch. Upon reorganization of the Institute in 1972, he was assigned to the Review Branch of the Division of Extramural Affairs.

He was appointed chief of the Program Projects Review Section in 1976. He has received a number of meritorious service awards during his service with NHLBI. He serves on several committees and participates in educational programs for the NIH staff.

Upon retirement Dr. and Mrs. Merrick will return to Columbia, Mo., where he intends to devote significant amounts of time to contemplative piscatorial studies and to the many other activities available in the academic environment. He intends also to visit their five children who are scattered about the U.S.
Cyclosporine Being Tested by NEI and LSU
To Improve Corneal Transplant Success Rate

A drug that may help to improve the success rate of corneal surgical transplants is being tested in a study underway at the National Eye Institute's Clinical Branch and the Louisiana State University Eye Center.

Although corneal transplantation is considered to be the most successful transplant operation known—corneal grafts have restored sight to hundreds of thousands of people—5 to 20 percent of the implanted grafts are rejected.

The drug to be tested—cyclosporine—has been used to prevent rejection of heart, kidney, and liver transplants, but has never been tried in the United States with patients receiving corneal grafts to replace their own damaged or defective corneas. The cornea is the transparent, curved tissue at the front of the eye that helps a person to focus or see clearly.

Study investigators will evaluate cyclosporine in patients who are undergoing corneal transplantation but are known to be at high risk of rejecting the graft because of previous corneal graft rejection.

Half of the patients will receive standard post-transplant treatment with systemic steroids (by mouth), and half will receive oral systemic doses of cyclosporine. (All the patients will use steroids topically. Results from each of the two groups then will be evaluated to compare the safety and efficacy of the two different drug regimens.

The new drug, it is hoped, will prove to be more effective in preventing graft rejection and cause fewer harmful side-effects than steroids, which have been implicated in the development of glaucoma, cataracts, high blood pressure, diabetes, osteoporosis, and suppression of the patient's total immune system.

Cyclosporine, on the other hand, appears to inhibit only a portion of the patient's immune system. Unlike other immunosuppressive agents, this drug does not cause a significant reduction in the number of white blood cells of the B type, which are needed to produce infection-fighting antibodies. And though cyclosporine can be toxic to the kidneys and liver, the drug will be given for such a short time in this study it is believed that any side-effects would be reversible.

To be eligible for this first clinical trial of cyclosporine in corneal transplant patients, candidates must have had at least two previous corneal transplants which failed to survive, or there must have been one failed graft in a person with corneal problems affecting both eyes. The conditions, for which a corneal transplant may need to be performed include: congenital abnormalities, scarring due to injury, and corneal dystrophies such as keratoconus (a protrusion of the center of the cornea).

Not eligible for the study are persons who have uncontrolled glaucoma, insulin-dependent diabetes, uncontrollable high blood pressure, severe osteoporosis, convulsive disorders, liver or kidney disease, severe chronic obstructive lung disease, or a history of malignancy.

To be considered for the study—which is cosponsored by Sandoz, the manufacturer of cyclosporine—patients must be referred by a physician. Referrals may be arranged by calling Drs. Manuel Dutry, Leslie Fujikawa, or Robert Nussenblatt, at (301) 496-3123.

According to the Eye Bank Association of America, about 25,000 corneal grafts were transplanted last year in the United States. The vast majority of them survived, restoring useful vision. Even so, graft rejection is common in certain high risk patients, and once the first graft fails to "take," rejection of the second graft is more likely.

Dr. Wm. Zukel, NHLBI, Awarded Honorary Degree

Dr. William J. Zukel, deputy director of the Division of Heart and Vascular Diseases, NHLBI, has been awarded the honorary Doctor of Sciences degree by the Council on Higher Education, University of Puerto Rico School of Medicine.

The award was conferred for Dr. Zukel’s "contribution to humanity in the area of science and health," and because he has been "instrumental in promoting research, especially in the field of cardiovascular diseases, and particularly in helping the people of Puerto Rico.

He was presented the honorary degree by the president of the University of Puerto Rico at the graduation ceremonies of the medical sciences campus held in San Juan on June 7.

Dr. Zukel began his career at NIH in 1957 when he was appointed assistant director of the then National Heart Institute. He has held a succession of posts within the Institute and has been the prime mover in planning and coordinating several of the major international epidemiologic studies and clinical trials carried out by NHLBI.

He was awarded the PHS Meritorious Service Medal in 1974, and the Distinguished Service Medal in 1983.

A native of Massachusetts, Dr. Zukel received his M.D. degree from Hahnemann Medical College in Philadelphia, and his doctorate in public health from the London School of Hygiene and Tropical Medicine. He is a member of numerous professional societies and has published extensively.

Win Welsh, Secretary, OC Retires After 16 Years

Winfred H. Welsh, secretary to the Associate Director for Communications, OD, retired on Aug. 2 after 16 years of Federal service.

Win, as she is affectionately called by her colleagues and friends, has worked in the Office of Communications for the past 6 years.

A native Washingtonian, Win graduated from the Washington School for Secretaries and obt
Three DRG Staff Members Retire With Combined Federal Service of 71 Years

Three members of the Division of Research Grants, Dr. Lottie Kornfield, Irene Lyddane of the Referral and Review Branch and Dolly Douglas of the Statistics and Analysis Branch, recently retired with combined Federal service of 71 years.

Dr. Kornfield, executive secretary of the Immunological Sciences Study Section since 1974, entered Federal service in 1963, as a research microbiologist with the Naval Radiological Defense Laboratory in San Francisco.

She received her Ph.D. degree in 1960 from the University of Chicago, where she was a National Science Foundation Cooperative Graduate Fellow.

Dr. Kornfield plans to return to the San Francisco area where she lived until she came to Washington.

Ms. Lyddane, a grants clerk in the Referral Section, spent her entire career of 23 years in DRG. First, she worked as a clerk in the fellowships committee of the Career Development Review Branch and after the branch was abolished, in the Referral Office.

She received several performance awards during her career and says she was lucky to work with nice people over the years.

She plans to take 2 months to visit members of her large family and afterwards, work part-time at the National Cathedral.

She also hopes to have time to return to commercial art which she studied earlier. An avid sports fan, she plans to watch various games, including upcoming Redskins games.

Ms. Douglas, a program analyst in the Report, Analysis, and Presentations Section, started her Federal career as a secretary in the Department of Defense where she worked for 11 years before coming to DRG in 1971.

In DRG, she was involved in providing statistical data on NIH extramural activities for publication in the NIH Data Book and the Extramural Trends, two resource publications used by NIH management and others.

Ms. Douglas plans to travel and pursue her many hobbies which include art and antiques collecting.

Three Members Appointed to NIGMS Advisory Council for 4-Year Terms

Dr. Theodore R. Sherrod, professor of pharmacology at the University of Illinois College of Medicine in Chicago; Ms. Barbara A. Gill, state senator for Maine's 32nd District (Portland) and Dr. Oliver Smithies, professor of genetics and medical genetics at the University of Wisconsin in Madison, have been appointed to the National Advisory General Medical Sciences Council for 4-year terms.

The Council, which meets three times a year, is composed of leaders in the biological and medical sciences, education, and public affairs. Its members review applications for research and research training grants and make recommendations.

The National Institute of General Medical Sciences funds research and research training in the basic biomedical sciences. This support enables scientists at universities, medical schools, and research institutions throughout the country to work to expand knowledge about the fundamental life processes that underlie human health and disease.

Dr. Sherrod is a pharmacologist with research interests in cardiovascular and renal pharmacology. He received an A.B. degree from Talladega College, an M.S. degree in organic chemistry from the University of Chicago, and his Ph.D. and M.D. degree from the University of Illinois College of Medicine. He has served on the faculty of the University of Illinois College of Medicine since 1944.

He also serves on numerous committees including the University's Hospital's committee on pharmacy and therapeutics and on the board of directors of the Chicago Lung Association and of the John Crear Library in Chicago.

He holds membership in the American Society for Pharmacology and Experimental Therapeutics and the American Society for Experimental Medicine and Biology.

Ms. Gill is the special projects coordinator at the Osteopathic Hospital of Maine in Portland. She is also a member of the Maine legislative council, and serves on the national conference of state legislatures and the council of state governments, eastern regional conference.

As a state legislator, she is an active participant in the HHS National Center for Health Services workshops dealing with various health issues. Ms. Gill is currently a member of the board of directors, and a former president, of the St. John's Federal Credit Union of South Portland, Me.

She attended the University of Southern Maine and trained as a laboratory technician at several hospitals in Maine. Ms. Gill is former owner and manager of Gill's Leader Drug Inc.

Dr. Smithies is a geneticist studying at various aspects of the regulation of gene expression. He received his B.A. degree in physiology and M.A. and Ph.D. degrees in biochemistry from Oxford University.

Since 1960, he has been on the faculty at the University of Wisconsin at Madison, where in 1971, he was appointed the Leon J. Cole professor of genetics and medical genetics.

In 1980, Dr. Smithies became Hilldale professor of genetics and medical genetics. In 1971, the University of Wisconsin at Madison, where he received his B.S. degree in biology, M.A. and Ph.D. degrees in biochemistry from Oxford University.

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He is recipient of many other honors including the Founders Award of the Electrophoresis Society and the Karl Landsteiner Memorial Award of the American Association of Blood Banks in 1984. Dr. Smithies is a past president of the Genetics Society of America.

R&W Plans Weekend Sail

Join R&W for a weekend sailing trip on the Chesapeake Bay, Aug. 23-25. Sailboat rental, captain, cook, breakfast and lunch on Saturday and Sunday are included in the price of $165 per person.

Participants will meet at Annapolis Harbor Marina between 6 and 7 p.m., Friday, to load gear onto the boats. On Saturday they will sail to St. Michael's to enjoy this quaint historic town and will return to Annapolis on Sunday at approximately 5 p.m.

Sign up at the R&W Activities Desk, Bldg. 31.
New Technique, Funded by NIGMS, Being Developed To Quickly Identify Disease-Causing Microorganisms

When a patient arrives at a hospital suffering from a severe infection, doctors need to start treatment immediately. Often they must do this without knowing—for at least a day or, in many cases, much longer—what is causing the infection. The choice of treatment is based on the patient’s symptoms and history, and on the physician’s experience. Since various disease-causing fungi, bacteria, and viruses respond differently to different modes of treatment, it is important that the physician choose well.

In some cases, the clinical microbiology laboratory—part of the hospital responsible for the isolation and identification of microorganisms—can, by microscopic examination of the patient’s blood specimen or other body fluids or by how such a sample reacts to certain chemical staining techniques, make a relatively speedy report.

Infectious Organisms

Also, many infectious organisms can be cultured, or grown, from the specimen in less than a day and then identified using one of many different assay systems that are available. These systems may take a few hours to pinpoint the cause of an infection, providing there are a large number of organisms in the specimen.

However, there are many organisms, such as those that cause meningitis, gonorrhea, and Legionnaire’s disease, that are difficult to grow or grow very slowly. Identification of some infectious agents can take weeks.

At Los Alamos National Laboratory in Los Alamos, N.M., National Institute of General Medical Sciences grantee Dr. Gary Salzman and co-investigator Dr. Charles Gregg, are working on such a system which could identify microorganisms in minutes without first requiring that they be isolated and cultured.

At present, those assay systems most widely used to identify microorganisms depend on “tagged” or labeled substances that bind specifically (form a chemical union) with a particular infectious organism or an antibody produced by the host to that organism. An antibody is tailored to fit the infectious organism or antigen the way a key fits a lock.

Binding Step Essential

The binding step is the essential event needed to identify the microorganism. After the antibody binds to the antigen portion of the organism, the unbound matter is washed out of the specimen and the assay is performed.

The specific tag used may be a radioactive chemical, a fluorescent dye or an enzyme. The organism with its tagged antibody can be detected with an assay designed to specifically measure radioactivity, fluorescence or enzyme activity.

Although these so-called immunoassays for rapid identification of the cause of an infection have been greatly improved recently, they still take several hours to complete.

Dr. Salzman’s system, which grew out of his basic studies of the scattering of light from cells, involves principles quite different from any previously used in clinical microbiology. He employs a technique known as MLS (for multiparameter light scattering) to analyze how specimens interact with polarized light.

Light from a laser passes through a polarizer and then through a modulator. This bends the polarized light to the right and left in a circular fashion.

When a biological sample is placed in the device, the pattern of light scattered by the sample is measured by a spectrometer (an optical instrument for measuring light). The device can use different signal frequencies, each of which brings additional information to aid in identification of the organisms in the sample.

Dr. Salzman believes his system works by recognizing the “packaging” of the genetic material that is unique for each microorganism. Since the genetic material of biological specimens like bacteria, fungi, or viruses is asymmetric, it interacts differently with polarized light coming from different directions.

By making many observations and using a computer to tally the results, Dr. Salzman’s system has shown remarkable ability to distinguish among very closely related organisms like the viruses from various forms of influenza, dengue fever (a tropical disease), and encephalitis.

Dr. Salzman’s present device is a stationary instrument in which the viruses and bacteria in the specimen are identified in a test tube. He is now planning to combine the MLS device with a flow cytometer—a machine that sorts cells extremely rapidly—in order to determine in a matter of minutes both the identification and an estimate of the relative quantities (numbers) of microorganisms in samples which contain many different types of organisms, as do most clinical specimens.

Diagnosis Time Shortened

The shortened time it will take to make a diagnosis with this system should prove valuable in the treatment of many diseases, including spinal meningitis, septicemia, pneumonic plague, and Legionnaire’s disease, illnesses for which prompt diagnosis is particularly important for effective therapy.

In some situations it might prevent unnecessary invasive intervention, such as the performance of a Cesarean section in a pregnant woman who has lesions resembling herpeses and who is about to deliver a child.

In addition to possibly reducing the incidence of death or permanent damage due to infection, such rapid diagnosis may shorten the time spent in the hospital, and help hospitals better control the spread of infection.

Practical development of the device for clinical use will be supported by Mesa Diagnostics, a private firm which hopes to have this system ready for marketing by 1987.

Doris Brody

Retirement Planning Program

The Recruitment and Employee Benefits Branch, DPM, is offering another Retirement Planning Program for NIH employees on Oct. 31 and Nov. 1. A Personnel Bulletin will be distributed desk-to-desk giving more detailed information.

The NIH Record
How Does a Fruit Fly Know What Time It Is?

Nature is crowded with examples of the effects of biological clocks. Migration, hibernation, and courtship are dependent on these timing systems to a large extent. A biological clock or biological rhythm, can be defined as an innate process in an organism that causes regular cycles of function or behavior. These cycles may be 24 hours (circadian), or longer.

Scientists know that biological rhythms are innate because they exist in the absence of environmental cues, such as the 24 hour day/night cycle.

Scientific literature contains many references to animals that change their behavior only slightly even if they are in constant light or constant darkness for extended periods of time. For example, microorganisms called Gonyaulax that use sunlight for energy, have a biological clock that makes them active during daylight hours. Yet when Gonyaulax were kept in constant light for several weeks, they maintained their usual cycle of energy acquisition as if they were still experiencing daylight only every 12 hours.

From this and many other examples, researchers know that these rhythms have a biological basis.

Although biological clocks occur in numerous species (including humans) and have been studied for more than 30 years, scientists know little about their biological or physiological basis.

In some organisms scientists have found certain areas of DNA (one component of chromosomes) that contain genes which, when they undergo mutations, change the individual's biological rhythms. Isolation of the mutations that change biological rhythms has made analyses of these phenomena at the molecular (DNA) level possible.

National Institute of General Medical Sciences grantees Drs. Michael M. Rosbash and Jeffrey C. Hall, and their colleagues at Brandeis University in Waltham, Mass., are studying genetic mutations that disturb circadian rhythms in Drosophila melanogaster (fruit flies).

Studies of the genetic basis of behavior, such as circadian rhythms, in lower animals can provide information useful for human applications. Researchers study invertebrates—members of the animal kingdom that lack a backbone—such as Drosophila because they are less complex and better understood developmentally and genetically than any vertebrates. Eventual understanding of how genetic factors affect complex behavior in higher organisms, including humans, depends largely on the progress scientists make now, studying invertebrates.

Dr. Rosbash and his colleagues are working with one area of the fruit fly chromosome (one of the four types of fruit fly chromosomes) called the "per" (period) locus. (A locus is the place on a chromosome where any form of one particular gene resides.) Two of the most studied behaviors known to be changed by "per" mutations are circadian rhythms of fly activity (flies normally are active during the day, not at night), and the rhythmicity of male courtship songs. Different mutations at the "per" locus will lengthen, shorten or abolish these biological rhythms.

From observation, scientists know that when "per" DNA is broken in particular places, predictable changes in the fruit fly's biological rhythms result. To learn more about these effects of "per" mutations, the scientists used recombinant DNA methods to transfer different subsections of "per" DNA from normal flies to mutant flies that lacked circadian behavior. Dr. Rosbash and his coworkers hoped to restore biological rhythms to the mutant flies.

The scientists found two particular overlapping "per" DNA fragments each of which restored circadian behavior to mutant flies that had lacked it. This was significant because it was the first time that DNA transferred from one higher (multicellular) organism to another effectively "rescued" a mutant by restoring its normal behavior. Moreover, the scientists had no knowledge of the gene product (protein specified by the DNA) that caused this "rescue," which complicated the experimental strategy. Exactly how these transferred DNA sections (or, the proteins that they represent) affect circadian rhythms remains to be determined.

Another goal of Dr. Rosbash's research is to determine the genetic regulatory components that turn circadian behavior on and off, and how this DNA sequence has diverged in the evolution of the various species of Drosophila. These studies will involve transfer of the normal "per" DNA from another species of fruit fly, Drosophila simulans, to see if it will restore biological rhythms in mutant Drosophila melanogaster. The scientists are also interested in whether the mutant fly will regain biological rhythms characteristic of its own species (melanogaster) or those of the donor fly, Drosophila simulans.

Dr. Rosbash believes that evolutionary divergence may account for differences among the various species' biological rhythms.

Dr. Rosbash's research is an important first step toward determination of the genes that are the physical basis of the organisms' ability to live by internal clocks. His research promises significant breakthroughs in understanding the genetic regulation of behavior and development. -Sandy Hecker

Literature Searches

Current bibliographies on subjects of widespread interest are available without charge from the National Library of Medicine's Reference Section. The bibliographies were produced through NLM's computer-based MEDLARS system and contain references from recent medical journal literature.

A complete list of available Literature Searches is published each month in Index Medicus and Abridged Index Medicus.

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

The newly available bibliographies follow:


The NIH-based Bethesda Medical Chapter of the National Contracts Management Association has recently begun its second year and has elected officers installed by Jack Higgins, retiring National President. Officers are (l to r): Betty Nordan, treasurer; Claire Marwick, president; Mr. Higgins, installing officer; Gloria Dahl, vice president; Sharon Miller, secretary. (Curtis Tate, chapter director, is not shown.) Meetings are held at lunchtime, the third Wednesday of each month, at the National Library of Medicine. Further information may be obtained by calling Claire Marwick, (301) 496-4637.
The World Health Organization (WHO) recently convened a panel of experts to discuss research opportunities in the fields of immunology and the neurobiology of aging. The National Institute on Aging was represented by Dr. Zaven Khachaturian, chief, Physiology of Aging Branch, Biomedical Research and Clinical Medicine Program, and Dr. William Adler, chief, Clinical Immunology Section, in the Clinical Physiology Branch of the Institute’s Gerontology Research Center in Baltimore.

The report developed from this meeting, edited by Dr. Adler, outlines areas of basic and clinical research in immunology and neurobiology that would be of greatest interest to researchers on aging in the international scientific community. In particular, the report emphasizes the need for standardized technology and animal resources as well as for repositories to store serum, tissue samples, and biological specimens.

As the number of elderly persons increases worldwide, WHO is interested in developing proposals designating priority areas in aging research which can be coordinated on an international scale, and for which funding sources can be identified and developed.

The report of this meeting will be presented to the WHO Advisory Committee on Medical Research in October. During July, it was presented, in part, to a committee of the U.S. Senate.

Native Americans Announce Indian Awareness Program

NIH Native Americans have announced the 1985 American Indian awareness program to be held Sept. 25-27.

Programs will be held in Masur Auditorium starting at 11:45 a.m. each day. Speakers will include: on the 26th, Ray Halbritter, a tribal leader of the Oneida Nation of New York, on “the Iroquis Confederacy”; on the 26th, Wanda Wood, president of the Maryland Chapter on the North American Indian Women’s Association and its objectives; and on the 27th, Mitchell Bush, president of the American Indian Society, Washington, D.C. on “The Urban Indian.”

The well-known Apache Crown Dancers from the Mescalero reservation in New Mexico will perform traditional Apache songs and dances between 12:40 p.m.-1:15 p.m. on all three days.

Indian Arts and Crafts including bead work, pottery, silver, leather craft and traditional dress will be on display in the Medical Center Information Office’s balcony museum as well as the Bldg. 31A patio between 10:30 a.m. and 2 p.m. on all three days.

Arts and crafts persons will be happy to answer such questions concerning their displays as:
- Why an Indian never closes a circle in his or her art or craft work?
- What is proper tepee etiquette? Why is it still observed during ceremonies today?
- What do the Eagle, Bear, Buffalo, Owl and other animals mean to an Indian, even today?

R&W Plans Trip to Hilton Head

R&W is planning a trip to Hilton Head, S.C. for Veterans Day Weekend.

The bus leaves NIH on Friday, Nov. 8, at 7 a.m. and leaves S.C. for the return trip on Monday, Nov. 11 at 7 a.m.

The cost is $130 per person (based on double occupancy) and includes three nights at the Hyatt Hotel on Hilton Head Island and round trip transportation.

Sign up at the R&W Activities Desk, Bldg. 31.

Two NIADDK Program Directors Share American Diabetes Association Award

Jean Curran, diabetes research program director in the National Institute of Arthritis, Diabetes, and Digestive and Kidney Diseases (NIADDK), and Dr. Keath K. Krueger, NIADDK diabetes centers program director, shared the American Diabetes Association’s Charles H. Best Medal this year for outstanding service to the field of diabetes. Five other individuals were coreipients of the award, among them, Dr. Lester B. Salans, former NIADDK Director.

The medals—named for the codiscoverer of insulin—were presented at the 45th annual meeting of the American Diabetes Association (ADA) in Baltimore in June.

Donald Wheldon and Gordon Tomkins. Following 2 years in the extramural program of NIGMS, Ms. Curran became assistant endocrinology program director, NIAMD, in 1969 and diabetes research program director in 1977.

For her management of the diabetes program during these years, Ms. Curran received an NIH Award of Merit in 1981, and the NIH Director’s Award in 1985 for “exceptional achievements in advancing the mission of the NIH by fostering biomedical research on diabetes mellitus.”

The ADA award for Ms. Curran comes just before her retirement after 30 years at NIH.

Dr. Krueger came to NIAMD in 1963 as scientific communications officer in the Office of the Associate Director for Program Analysis and Scientific Communication. She moved to the Institute’s extramural program in 1974 as diabetes research program director and became director of the Diabetes Centers program when it was created in 1977.

In addition to her program positions, she was executive secretary of the National Commission on Diabetes from March 1975 to September 1976 and has served as the Executive Secretary of the Diabetes Mellitus Interagency Coordinating Committee since its inception in 1974.

In recognition of her performance in carrying out these simultaneous and demanding responsibilities, Dr. Krueger received a PHS Special Recognition Award in 1976 and the NIH Award of Merit in 1984.

Bowling League Meets Aug. 28

The next meeting of the NIH mixed bowling league will be held on Wednesday, Aug. 28, at 7 p.m. at Brunswick River Bowl. The first league play will begin Sept. 4 at 6 p.m.

To sign up for a team or for more information, call Ralph Isenberg, 496-3609.

Instead of loving your enemies, treat your friends a little better. —E.W. Howe
Updated Animal Care Guide Available for Distribution

A revised edition of the Guide for the Care and Use of Laboratory Animals is now available for distribution, according to Dr. William Gay, director of the Animal Resources Program of the Division of Research Resources. Since the initial edition in 1963, the Guide has become widely recognized as the primary reference on standards of animal care in scientific institutions.

Last revised in 1978, the Guide was updated recently by a special committee of the Institute of Laboratory Animal Resources of the National Academy of Sciences to reflect the policy of the Department of Health and Human Services (DHHS) on the care and use of animals used in research experiments.

Besides improving its bibliography, the latest edition makes recommendations for new methods of cage ventilation and other housing requirements, including a few revisions in cage sizes.

The new version of the Guide also goes beyond previous editions in adding specific references to support their recommendations and defining more specifically many of their recommendations.

The Guide includes, as an appendix, a statement of principles developed by the Interagency Research Animal Committee (IRAC), a group of Federal agencies that use research animals in the programs they support. In addition to NIH, other members of IRAC include: Departments of Agriculture, Defense, State and Interior; the Environmental Protection Agency; NASA; the Air Force; the Army; and the Veterans Administration.

Since the Guide first appeared, more than 300,000 copies have been distributed to all types of scientific institutions. A copy of the latest edition of the Guide may be obtained from the Office of the Deputy Director of NIH. (Continued on Page 11)
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lal. As far as the institutions that are affected by it, there is no difference.

Q. So, the Public Health Service as a whole has delegated authority from the Secretary (of HHS) to do certain things.

A. Yes. Our policy actually constitutes conditions under which awards may be made. In other words, if an institution accepts an award it accepts the responsibility to treat the animals in a humane way consistent with our policy.

Q. And of course you could suspend a grant or withdraw it out for violations involving animals.

A. Yes, we have very strong sanctions available to us. We (NIH) can either suspend a portion of an award, the entire award, or in an extreme case, we can suspend all of an institution's awards involving animals. And we have recently done the latter in one case. We have done it in a major institution.

Q. But the U.S. Department of Agriculture has another kind of authority—similar—but with different kinds of inspections and different kinds of penalties?

A. Yes. The Department of Agriculture has responsibility for implementing the Animal Welfare Act. The Animal Welfare Act pertains to most animals with the exception of rats and mice. And since somewhere in the range of 90 percent of all research animals are rats and mice, there are many institutions that are not directly supervised or inspected by the Department of Agriculture.

Secondly, the Animal Welfare Act specifically excludes research activities so that our policy really affects the care of animals including rats and mice which are not covered by USDA as well as the use made of animals in a research context which is not covered by USDA. Nevertheless, we do work closely with them.

Q. Coming back to NIH, your office—OPRR—is that the one that decides whether an investigation should be made. On what basis do you decide that?

A. Well, whenever we receive an allegation of noncompliance to a Public Health Service policy we initiate an inquiry. If that inquiry leads us to believe there may be serious problems then we elevate the inquiry to a full-scale investigation.

Q. If you have to go to a full-scale investigation, who actually conducts it? Do you delegate it to some inspectors or investigators?

A. Normally, this office, OPRR conducts it but we borrow personnel from various institutes and we frequently contract with outside experts to assist us.

Q. So whoever the investigating knows what to look for and how to assess it?

A. Yes, that is correct.

Q. There's been some controversy and a charge that there's been a delay in the University of Pennsylvania head injury investigation. How long did it take and was it longer than ordinary and was there justification for the length of it?

A. It's hard for me to say what is ordinary because some investigations are very brief. In fact, most others have taken as long or longer than the University of Pennsylvania. The reason for the extended investigation at the University of Pennsylvania was that the principal evidence that can be used was evidence. And the people in possession of that information declined to turn it over to us for nearly a year.

We received that evidence on May 23 of this year and it consisted of approximately 80 hours of videotape, which had to be carefully analyzed. So between May 23 and mid-November most of that tape was reviewed up to five times and documentation was made on every single animal and the treatment of every single animal; some 47 animals were depicted on the tape and we then completed a report based on our analysis of the entire set of tapes. We think the investigation was really completed in a rather short time once the tapes were in hand. But the evidence was stolen one year prior to its being turned over to the NIH.

Q. Assuming you find there is some violation of the rules and regulations in a given project—and that it warrants some kind of penalty—what are the different kinds of things you can do and on what basis do you do them?

A. Well, we try to make the punishment fit the crime. There are two categories of noncompliance: the first and the more common, is that an institution's administration of its animal policy or facilities has fallen below acceptable standards. In that case, we hold the institution responsible for bringing the policies or facilities into compliance with the Public Health Service policies.

In a few cases, the facilities and the institution may be functioning properly but the investigator has broken the rules. In which case, we try to make the sanctions pertain to a given project or to a specific investigator since it doesn't seem to be the entire institution that's out of line.

Q. NIH has adequate, ample power to remedy malpractices when it finds them.

A. Yes, but we feel that our investigations have to be very carefully carried out because in the event that we have negative findings, the accused have the right to appeal. Those appeals are reviewed according to very rigorous administrative procedures and consequently the evidence we have to have must be conclusive. So we cannot—simply on the basis of casual allegations—bring about sanctions. If we can develop demonstrable evidence, then we take appropriate action. These inquiries and investigations are carried out, at least from our point of view, in a confidential manner.

Frequently, the institution or the investigator will volunteer to take corrective steps to the press, so not all of them are carried out in a confidential manner. But, so far as we're concerned they're to be treated confidentially and the results are made public only when we have completed the investigation.

Q. So if there is any statement before conclusion of the investigation it would be on the part of the individual or institution, not NIH.

A. That is correct. It should be made clear that in the implementation of our policy we rely primarily on the statement of each institution that they will be in compliance with the policy and we accept that on good faith. We're not quite so naive as to think that simply putting something on paper always means that institutions are going to be in compliance. Consequently we have a variety of site visits to randomly selected institutions.

We've covered approximately 18 of these since 1983 in addition to investigations for cause and we are continuing to carry out random site visits. That's still a small percentage of a total number of institutions but the word is out in the community that any institution is subject to receiving a visit virtually unannounced.

When we visit a site, what we look at are administrative records going back three years, minutes of the animal care committee going back three years. We interview investigators, veterinarians and members of the Institution's Animal Care and Use Committee. We look at the facilities, we check the records of what food was procured, when cages were procured and check these against the arrival of animals and so on.

What our site visits concentrate on is not particular shortcomings but the general administration of the program and that's the difference from USDA. USDA looks for specific shortcomings: the cage is dirty or rusty, the cagewasher doesn't work, etc.

What we look at is, does the institution have an appropriate administrative structure to deal with the problems that inevitably are going to arise in an animal program? Do they have a good engineering staff so that if something breaks it will be immediately fixed? If the plumbing gets plugged with animal hair will it be corrected immediately? Do they have a way of obtaining a new cagewasher if the old one breaks down?

Is there central procurement so that an investigator can order animals and not have them waiting out on the loading docks in wooden crates because the cages haven't arrived yet?

Those are the kind of questions that we look at: we try to get at the root of the matter.

Q. Under new regulations with more random site visits and an intensified education program, what specific things can you think of that will make it more likely there will be improved future care and use of laboratory animals?

A. Well, I think ultimately, we need to get away from a regulatory stance and stress an educational effort and to that end we held a national symposium last year. We have followed up with regional meetings around the country. We have begun this process and have scheduled 8 regional meetings in this calendar year and will continue to hold these regional meetings.

We will try to reach investigators, administrators, veterinarians and other people who have responsibility for running a good program. And we think ultimately the way to make sure that we have good programs is to sensitize people. We feel we would prefer not to do that through disciplining them or punishing them but rather through educating them. We do not consider ourselves so much a regulatory office as an educational and sensitizing office and we think that is ultimately the way to make something happen.

"Distinguished Nurse Lecture' Announced by CC Nursing Dept.

The Clinical Center Nursing Department has announced a new lecture series. "The Distinguished Nurse Lecture." The series will provide a national forum for discussing important issues in contemporary nursing.

First speaker for the series will be Dr. Jean E. Johnson, R.N., a nationally known scholar in nursing with extensive research experience in patient care.

First lecture of the new series will be presented at 9 p.m., Wednesday, Oct. 16, at NIH's Clinical Center, ACRF Amphitheater. A reception will follow. For further information, call (301) 496-6012.

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NINCDS Mounts Clinical Trial of Cyclosporine
As Curb on Progressive Multiple Sclerosis

By Lynn J. Cave

A clinical trial of an immunosuppressant drug that may stabilize patients with chronic progressive multiple sclerosis has begun at NINCDS and 11 other centers throughout the country.

Cyclosporine, the drug under study, selectively inhibits one type of white blood cell in the immune system which is the body's main defense against foreign invaders. Normally, these cells detect bacteria, viruses, or transplanted organs they signal other immune system cells to mount an attack. Cyclosporine blocks one of the signals that is crucial to the formation of immune cell armies.

Since the mid-1970s, transplant patients have been receiving cyclosporine to prevent their immune systems from rejecting new organs. Recent evidence suggests multiple sclerosis patients may have an abnormal immune response in which the immune cells attack myelin, the coating on nerves in the brain and spinal cord.

"Since cyclosporine works so well at decreasing the immune response in transplant patients, it is reasonable to assume that it may suppress any possible immune system attacks on myelin," says Dr. Henry McFarland of the Institute's Neuroimmunology Branch, who is running the drug trial at the NINCDS center.

In multiple sclerosis the myelin sheath insulating nerve cells in the central nervous system is destroyed and replaced by scar tissue. People with multiple sclerosis experience a wide variety of symptoms depending upon which nerve cells are affected. The most common problems are weakness, numbness, and difficulty with coordination.

For the majority of patients, multiple sclerosis symptoms wax and wane. Approximately 30 percent, however, have symptoms that steadily worsen without remission. It is these "chronic progressive" patients on whom cyclosporine is being tested.

In small, preliminary trials completed last year in Europe, the drug appeared to stop advancement of the disease in chronic progressive patients. The promising evidence of a stabilizing effect convinced Sandoz Ltd., the Swiss pharmaceutical company that patented cyclosporine, to sponsor a larger trial.

Each center in the current study will follow 40 to 60 patients who will be randomly assigned to take a placebo or cyclosporine for 2 years. Neither the physicians nor the patients will know who is receiving which treatment. Medication and funds to conduct the study are being supplied by Sandoz.

Dr. Henry McFarland of the NINCDS Neuroimmunology Branch evaluates the coordination of a patient participating in the cyclosporine trial.

"This is a rigidly designed, definitive trial," says Dr. McFarland. "It should provide a definite answer that yes, cyclosporine works for multiple sclerosis and let's treat more patients; or no, it doesn't work, so let's move on to something else."

Multiple sclerosis is difficult to treat because it is so unpredictable. One patient may be confined to a wheelchair, while another walks unaided. Symptoms that at times may be mild later can become debilitating, and serious symptoms can spontaneously improve giving patients false hope of a cure.

"Multiple sclerosis is unlike cancer, where in most cases you know how the disease progresses," says Dr. McFarland. "If you increase the survival time of a leukemia patient, you know you're successful. With multiple sclerosis it's difficult to tell whether you've been successful or the disease has improved on its own."

Although cyclosporine is perhaps the most effective and selective immunosuppressant known today, it is not without side effects. The drug has been known to affect adversely the kidneys' ability to cleanse life-threatening waste products from the blood.

Most studies, however, indicate that the drug's effect on the kidneys is temporary and that the cleansing ability of the organs will return to normal after the dose is lowered or the medication stopped. All patients participating in the Sandoz drug trial will receive kidney function tests to detect any toxicity.

Patients are still needed at the NINCDS center, says Dr. McFarland, but candidates for the study must be referred by their physicians.

Chronic progressive multiple sclerosis patients who have shown a general decline over the past year may be eligible for the trial. Since many of the neurological tests of disease progression rely on mobility, physicians should recommend candidates who are able to walk.

In addition to participating in the drug trial, patients at the NINCDS center will have the opportunity to be included in the Institute's ongoing research projects on multiple sclerosis.

Physicians involved in these projects will receive extensive tests to evaluate the functioning of their immune systems and will undergo brain scans with magnetic resonance imaging to determine the extent of myelin damage.

Physicians who wish to refer patients should contact: Dr. Henry McFarland, NINCDS, Neuroimmunology Branch, Bldg. 10, Rm. 5B18; telephone: (301) 496-1801.

Nominations for Hazen Prize
For Clinical Research Open

Nomination material is now available for the 1986 Lita Annenberg Hazen Awards for Excellence in Clinical Research.

Purpose of the awards is to encourage increased participation in clinical research by physician-investigators or teams.

Prizes totalling $100,000 are awarded: $50,000 (tax-free) to an outstanding physician-investigator and $50,000 for the support of a research fellow(s).

Nominations will be accepted until Feb. 28, 1986.

Candidates of international stature are sought. The 18-member awards committee invites nominations identifying a physician, or a team of physicians jointly conducting research, working at any institution in the world, whose achievements and potential for future breakthroughs in clinical research are outstanding.

Past recipients of the awards include: Jesse Roth, M.D., National Institute of Arthritis, Diabetes and Digestive and Kidney Diseases, 1979; Henry G. Kunkel, M.D., The Rockefeller University, 1980; Aaron B. Leiner, M.D., Yale University School of Medicine, 1981; Michael S. Brown, M.D., and Joseph L. Goldstein, M.D., of the University of Texas Southwestern Medical School, 1982.

An official nomination form plus details on how to submit a nomination are available from Dr. James F. Glenn, President, the Mount Sinai Medical Center; Chairman, The Lita Annenberg Hazen Awards Program; One Gustav L. Levy Place, N.Y., New York 10029 or call (212) 650-8532.

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