

"Still  
The Second  
Best Thing  
About Payday"

# The NIH Record

## Irving Weissman To Give NIH Lecture, Nov. 19

Hematopoietic stem cells, the ancestor cells in the bone marrow from which all blood cells are derived, are the subject of the NIH Lecture to be presented by Dr. Irving L. Weissman, professor of pathology and developmental biology and Howard Hughes Medical Institute investigator at Stanford University Medical School.

The lecture, entitled "Hematopoietic Stem Cells: Biological and Clinical Potentials," will be given in Masur Auditorium, Bldg. 10, on Tuesday, Nov. 19 at 3 p.m.

Weissman's talk will review the latest hematopoietic stem cell research—and the important implications of this research for AIDS, cancer, transplantation, gene insertion therapy, and for the study of the developmental biology of the immune system.

Weissman is an internationally recognized leader in the development and function of lymphocytes, the white blood cells responsible for the recognition of self from nonself. His research has focused on identifying the earliest blood cell in the bone marrow, and the ways these cells develop as they migrate to the body's other blood-forming tissues such as the thymus gland and spleen.

In 1988, Weissman and his colleagues reported a remarkable advance: a method to isolate stem cells in the mouse, a feat that had eluded researchers for more than 30 years. He has since shown that small numbers of these cells are able to produce a new immune system in mice whose bone marrow has been destroyed by radiation.

Weissman has also demonstrated that early human blood-forming cells, when transplanted into the immune-deficient SCID mouse along with human lymphatic and thymic tissue, will develop into differentiated cells and tissues capable of an immune response.

This mouse-human "chimera," a mouse with a human immune system, offers researchers a model to study human viral infections such as HIV. It also has enormous utility for the study of the signals that control the growth and differentiation—normal and

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## Dialogue with Sen. Mikulski Set Nov. 25 in Masur Auditorium

Sen. Barbara Mikulski of Maryland will engage in dialogue concerning issues of interest to NIH employees from 10 to 11 a.m. in Masur Auditorium, Bldg. 10, on Monday, Nov. 25. The dialogue with the senator will resemble a "town meeting" in its format, with questions from the floor. Dr. Bernadine Healy, NIH director, will host the meeting.

## Youngsters Become Medical Sleuths In NIH's 'Saturday Morning School'

By Anne Barber

Decked out in white lab coats and name tags, and armed with a list of disease symptoms, 18 junior high students (dubbed "docs") went searching through NLM's computers on a recent Saturday morning, hoping to find clues that would help them solve a medical puzzle. The mysterious illness sought by these adolescent sleuths is part of a 6-week educational program sponsored by NIH to interest youngsters in science.

"The concept of the program is to let these students learn the process of science," explains Dr. Jay Moskowitz, NIH associate director for science policy and legislation. "We invented a curriculum where an imaginary country is being devastated by a disease, but the disease itself is real. The idea is to get the kids to investigate and track down what the disease is. They will be given clues and hopefully," he says, "learn that mistakes and failures do not necessarily mean you cannot move on. Science is trial and error. You don't always achieve on the first try."

The BRASS (Biomedical Research Advancement: Saturday Scholars) program, created by Moskowitz and the new NIH Office of Science Education Policy under the direction of Bonnie Kalberer, grew out of the need to stimulate an interest in biomedical/life sciences in the Washington metropolitan area's sixth, seventh, and eighth grade students. The program, which includes scientists from NIH and ADAMHA, was designed by two local science teachers—Sandi Stempel and Nick Miller.

### Disability Awareness Yet Dim

## Playing Field Still Tipped Against People with Disabilities

By Rich McManus

Shopping centers have it. Art museums have it. Libraries have it. But Bldg. 31 lacks what these places have—automatic doors permitting access to the disabled.

The ninth annual NIH Disability Employment Awareness Program, held Oct. 24 in Wilson Hall, was full of such reminders of how many changes must be made before Americans with disabilities can have the same fair chance to work as others.

"Most NIH buildings don't have automatic doors, the cafeterias have turnstile entrances (unpassable by wheelchairs), many bathrooms aren't accessible, and there are transportation problems as well," reported Dr. Ron Geller, who in addition to directing NHLBI's Division of Extramural Affairs also chairs the NIH advisory committee for employees with disabilities.

"The doors, the restrooms, the provision of sign language interpreters—these are require-



'Saturday school' students search through NLM's databases for information. Offering assistance are reference staffers Martha Fishbell (foreground) and Pam Meredith.

During the Saturday morning sessions, the students will explore various aspects of biomedical and behavioral life sciences.

Stempel says the methods used in this teaching program will provide the students a backdrop for their learning—it includes geography, economics, sociology, as well as science. "It does not teach science in isolation," she states. "It introduces youngsters to what happens in the real world."

"In our model, the students are presented with a fictitious country, given demographic details, social characteristics of the inhabi-

(See BRASS, Page 6)

ments, not accomplishments," he said. "Having people (in NIH's workforce) who can use them is the accomplishment."

Geller had excellent news to report as well. NIH's participation in the Marriott Corp.-sponsored "Bridges" program for hiring and training high school students with disabilities has been a great success; 22 student-trainees have passed through the program since it

(See DISABILITY, Page 4)

## Raub To Be Honored Nov. 25 At Farewell Open House

NIH deputy director Dr. William F. Raub, who has accepted a post at the White House Office of Science and Technology Policy, will be honored at a farewell reception on Monday, Nov. 25, from 3 to 5 p.m. in Wilson Hall, Bldg. 1. All are invited to attend.

## NIH LECTURE

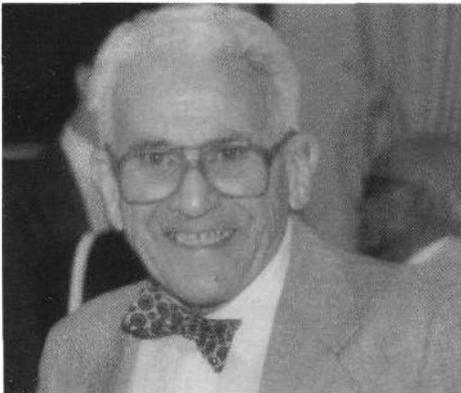
(Continued from Page 1)



Dr. Irving L. Weissman will deliver the NIH Lecture on Thursday, Nov. 19 at 3 p.m. in Masur Auditorium, Bldg. 10.

abnormal—of human immune cells, and how the immune system learns to tell “self” from “nonself.” Ultimately, this “SCID-hu” mouse may be the means by which the human hematopoietic stem cell is isolated and purified.

Weissman is a member of the National Academy of Sciences and the American Academy of Arts and Science. He received his M.D. degree from Stanford in 1965, and after postdoctoral studies in cancer biology, joined the Stanford Medical School faculty in 1969. In 1986, he was awarded an NIH Outstanding Investigator Award, and since 1987 has been the Karel and Avice Beekhuis professor of cancer biology at Stanford. In 1988, Weissman was awarded the Pasarow Foundation Award for his contributions to cancer immunology.—Greg Folkers □



Parasitology and tropical medicine researchers who have made notable contributions to the field will be honored in a new lecture series, the Gorgas Memorial/Leon Jacobs Lecture. Jacobs himself (above) will launch the series with a talk entitled, “A History of NIH Parasitology: People and Perspectives.” The program will be held in Bldg. 1, Wilson Hall at 3 p.m. on Wednesday, Nov. 27.

## FIC Announces Grant Program

A new small grants program to enhance research cooperation between United States scientists and their counterparts in Central and Eastern Europe, including the Soviet Union, and Latin American and Caribbean nations has been announced by the Fogarty International Center.

The new program, called the Fogarty International Research Collaboration Award (FIRCA), will promote collaborative research between U.S. scientists and those in the designated regions. About 35 such grants are expected to be awarded in fiscal 1992.

“We are already supporting visits between U.S. scientists and their Latin American collaborators in a modest way,” Dr. Philip E. Schambra, FIC director, said in announcing the program, “but this new small grants program provides a way to expand the collaboration and to provide longer-term stable support.

“In Eastern Europe, as a result of the end of the ‘Cold War’ and the rise of democratic movements in these countries, scientists are free to travel and collaborate with their western counterparts,” Schambra said. “Scientists in these countries are well trained but lack practical experience about many of the new techniques in biomedical research that are common in the West. They also often lack modern equipment necessary to utilize these techniques in their research. This new program will assist in filling these needs. Medical problems are becoming more complex and more expensive to solve. We need to employ the best minds available in seeking solutions.”

Each grant will provide up to \$20,000 a year to U.S. institutions for 1 to 3 years. These funds may be used for materials, supplies, and equipment for the collaborating foreign scientist’s research laboratory and for travel expenses for the U.S. principal investigator and/or the foreign collaborator and his or her research associates. No salaries or stipends are included.

Those eligible are U.S. scientists, through their institutions, who are principal investigators of NIH research project grants that will be active during the proposed grant award program. The deadlines for application are Oct. 1, Feb. 1, and June 1 of each year.

Further information and applications can be obtained from: Dr. David A. Wolff or Dr. Danuta Krotoski, International Research and Awards Branch, Fogarty International Center, Bldg. 31, Rm. B2C21, Bethesda, MD 20892, (301) 496-1653, fax: (301) 402-0779. □

## Preschoolers Needed

The NICHD seeks the help of parents and their healthy 4-year-old children to participate in a study of the development of language. For more information, call Anne O’Reilly, 496-6832. □



## Computer Training Classes

Classes	Dates
Convex Questions and Answers	11/18
Andrew File System	11/18
PC-DOS Advanced Topics	11/18-11/19
Network Services	11/19
Macintosh Dial-Up and Network Connectivity	11/19
BITNET	11/20
Intermediate PC-DOS	11/20, 11/22
Using MacVector	11/21
Using the Internet	11/21
Getting Started with DB2	11/21-11/26
Managing Data Effectively	11/22
Macintosh Software for the Scientist	11/25
Windows Sampler	11/26
LAN Concepts	11/26
Macintosh Networking with TCP/IP	11/27
Use of SAS at NIH	12/2-12/13
Running SAS Software in the PC-DOS Environment	12/3-12/5
ENTER BBS	12/3
Mainframe Services at NIH	12/4
CXbatch	12/5
Windows Optimization	12/6
Recurrent Problems in Data Analysis	12/9-12/13
Introduction to COMPRO Utilities	12/9, 12/11
Scripts and Buttons in FileMaker Pro	12/10
Introduction to PC - Mainframe Communication with ProComm Plus	12/10

Classes are offered by the Computer Center Training Unit, DCRT, without charge. Call 496-2339 for more information. □

# The NIH Record

Published biweekly at Bethesda, Md., by the Editorial Operations Branch, Division of Public Information, for the information of employees of the National Institutes of Health, Department of Health and Human Services, and circulated to nonemployees by subscription only through the Government Printing Office. The content is reprintable without permission. Pictures may be available on request. Use of funds for printing this periodical has been approved by the director of the Office of Management and Budget through September 30, 1992.

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## Zanvil Cohn To Give NIAID's Kinyoun Lecture, Nov. 21

By Karen Leighty

In the field of cell-mediated immunity, discussion of macrophages cannot go far without touching on the work of Dr. Zanvil A. Cohn. Because of the relevance of this work to NIAID's mission to further the understanding of infection and immunity, Cohn has been chosen as featured speaker for NIAID's Kinyoun Lecture, to be given in Lipsett Amphitheater, Bldg. 10, on Thursday, Nov. 21 at 4 p.m. The title of his talk is "Cell-Mediated Immunity: From Bench to Bedside."

The Kinyoun Lectureship was established to honor Dr. Joseph J. Kinyoun, whose Laboratory of Hygiene in the 1880's was an early precursor to NIAID. Kinyoun took his postgraduate training abroad at a time when researchers in Europe were beginning to shape the field of bacteriology into a tool for controlling infectious diseases. It was through Kinyoun's subsequent pioneering work with bacteria, along with the refinement of laboratory techniques needed to study them, that he became the first researcher to isolate the cholera organism.

Cohn, too, arrived on the biomedical scene at an auspicious time. He graduated from Bates College in 1949 and went on to Harvard Medical School, where he earned his M.D., *summa cum laude*, in 1953. His research interests in cell biology were spurred by technological advances occurring at that time. Much of the work was being done at the Rockefeller Institute, where researchers were making major inroads in the fields of electron microscopy, cell fractionation, and immunology. Cohn, meanwhile, was completing his internship and residency at Massachusetts General Hospital, followed by a stint at the Walter Reed Army Institute, where, from 1955 to 1957, he was chief of the division of rickettsial biology. The technological breakthroughs at Rockefeller, however, continued to entice him. In 1958, Cohn embarked on his Rockefeller career, beginning in the laboratory of the late Dr. Rene Dubos, known at the time for research critical to the development of antibiotics.

In one of his first projects, Cohn demonstrated that the exposure of polymorphonuclear leukocytes to bacterial endotoxin modified their metabolism and enhanced their ability to kill staphylococci. Since it was suspected that the killing mechanism centered in the granules that could be seen within the leukocyte, he focused on these elements. Within a short while, he was able to isolate the granules and show that they contained important cytotoxic proteins and digestive enzymes. With his coworker, Dr. James Hirsch, Cohn established how the process of degranulation works—how the granules fuse with phagocytic vacuoles, emptying their contents and initiating the



Dr. Zanvil A. Cohn of Rockefeller University will give the Kinyoun Lecture on Thursday, Nov. 21 at 4 p.m. in Lipsett Amphitheater, Bldg. 10.

killing and destruction of the pathogens.

Subsequently, Cohn and his group carried out similar studies of the other class of "cell eaters," the macrophages. As a result, the two collaborators described not only the origins and the differentiation of macrophages but also they discovered dendritic cells, a new class of immune cells.

It became clear that the macrophage is the central player in the cell-mediated immune system. Cohn and his colleagues elucidated how the macrophage undergoes endocytosis, a process in which the macrophage engulfs foreign particles by forming an inverted sac composed of the cell's outer membrane. By following the resulting endosome through the digestive process, the researchers were then able to show how the membrane is recycled. In what one researcher described as a 30-minute "phagocytic frenzy," macrophages are able to internalize and then recycle the entire surface area of the membrane. Later, Cohn's laboratory discovered that the macrophage's killing process involves hydrogen peroxide, a finding that has had a significant impact on the development of treatments for tumors and infections.

Macrophages are not only eaters; Cohn's laboratory has shown that they also release a wide spectrum of molecules that modulate the inflammatory and immune response. These versatile cells synthesize more than 70 such molecules, including arachidonic acid metabolites, the prostaglandins, and leukotrienes.

More recently, Cohn has been intrigued by the defective immune responses he has observed in patients with tuberculosis, leprosy, and AIDS. In these diseases, the lack of important lymphokines subverts the killing mechanism of the macrophage, allowing it to become a dangerous reservoir of pathogens. He

and his colleagues are now using recombinant lymphokines as possible immunotherapeutic agents to counter these deficiencies.

The biomedical community has long recognized Cohn's work and paid tribute with numerous honors and awards, including the Boylston Medal presented by Harvard University in 1961, the fifth annual Squibb Award given by the American Society for Infectious Diseases in 1972, the 1990 Joseph E. Smadel Award from the Infectious Diseases Society of America, and the Ciba-Geigy Award, which Cohn received from the International Society for Inflammation in 1990. He is a member of the National Academy of Sciences in addition to being a past member of the board of scientific counsellors for NIAID's Intramural Research Program. In addition, he is editor of the *Journal of Experimental Medicine* and serves as advisor or associate editor for the *Journal of Clinical Investigation* among others. □

## Healy To Make Extramural NIH Focus of STEP Forum, Dec. 4

NIH director Dr. Bernadine Healy will lead a STEP forum on "Current and Future Issues for the Extramural Program" on Dec. 4, from 1 to 3 p.m. in Wilson Hall, Bldg. 1. She will discuss her priorities and plans for the NIH extramural programs and answer questions from the audience concerning these activities.

The extramural programs of the NIH support a wide variety of basic and clinical research in the nation's universities and medical schools, as well as a broad spectrum of training for individuals wishing to pursue research careers. Dr. John Diggs, NIH deputy director for extramural research, will be the forum moderator.

The forum will be made available via closed circuit television to the Westwood Bldg., Rm. 428; the Federal Bldg., Rm. B1-19; and Bldg. 31C, Conf. Rm. 7. Those who cannot attend the forum in person are encouraged to take advantage of one of these alternative sites. Admittance to Wilson Hall will be on a first-come, first-served basis and will be limited to about 180 people. □

## Volunteers Needed at NHLBI

The Cardiology Branch, NHLBI, needs normal volunteers between ages 30 and 70 to participate in a study assessing the causative mechanisms of certain cardiovascular diseases. Volunteers must not be taking any medication. The study includes placement of a small needle in the brachial artery and takes approximately 4 hours. Participants will be paid. For more information call Cressie Kilcoyne, 496-8739. □

## DISABILITY

(Continued from Page 1)

started a year ago and several have been converted to permanent status.

Geller's good news earned him an audience with HHS secretary Dr. Louis Sullivan, who wanted to learn more about the Bridges program. Geller also had the honor of representing NIH at "ACCESS 2000," a recent OPM-sponsored conference at which NIH was one of only three agencies lauded for an exemplary program (Bridges) for accommodating people with disabilities.

There was still more good news. All around NIH, individuals are waking up to imaginative ways of employing workers with disabilities. Dr. Harry Mahar in the Division of Safety was praised for his work with Bridges students—he and his colleagues have



Dr. Ron Geller, who chairs the NIH advisory committee for employees with disabilities, gives a "state-of-the-union" address to those gathered for the disability awareness program in Wilson Hall.

even learned sign language to communicate more easily with deaf workers. Dr. Hynda Kleinman, chief of the cell biology section in NIDR's Laboratory of Developmental Biology, was recognized for a long history of hiring deaf employees and employees with disabilities; she also participates in a job training program through Gallaudet University. Art Lord in the Telecommunications Branch, ORS, has gone out of his way to assure that TDD machines (telephones for deaf people) function properly on campus and plans to install an intercom for people with disabilities at the Medical Center Metro station. Norm Osinski, director of acquisitions management at NIH, and Norm Mansfield, NIH associate director for research services, were also lauded for trying to make headway in the fight to make the campus accessible.

A sobering counterpoint, however, is that



Judge Leonard T. Suchanek, who gave the keynote address at the program, warned that equality is something to strive for, not something that is easily conferred. Photos: Ernie Branson

NIH "has a long way to go" before reaching its goal of employing people with disabilities in about 6 percent of its jobs, reported Joan Brogan, Disability Employment Program manager for the Division of Equal Opportunity.

"About 1 percent of the workforce at NIH has severe disability, and about 3-4 percent have self-identified disabilities," she said. "That's about the government average."

Roughly 11 percent of the United States workforce, representing about 43 million people, is disabled, Brogan noted. Only one-third of those individuals are able to find work.

"A study conducted by the Bureau of Census showed that 67 percent of people with disabilities ages 16 to 65 in this country who are able to work are unemployed," said keynote speaker Judge Leonard T. Suchanek, chief judge and chairman of the Board of Contract Appeals in the General Services Administration. "That is a national disgrace."

Blinded at age 5 in an accident and subsequent infection, the judge, a native of central Nebraska, nevertheless has risen to a prominent government post. In addition to being an

attorney and judge, he is also chairman of the Council on Accessible Technology.

"It's a pleasure to be here among colleagues who will work toward the progressive development of access for those with disabilities," he said. "I come to you not as a judge, or a chairman, but as a colleague who will join hands with you as we walk forward into an age when people with disabilities will be given the opportunities and rights of all Americans."

Suchanek reviewed a decade of progress in legislation protecting the rights of Americans with disabilities, culminating in passage last year of the Americans with Disabilities Act ("a landmark in the evolution of human society"), widely regarded as the watershed civil rights law covering people with disabilities.

Known as ADA, the law "is a tool, not equality itself," explained the judge. "It is a promise to be kept for empowerment of the disabled so that they can fulfill their potential as equal, as prosperous, and as welcome members of the mainstream of society."

He warned, "Government alone cannot enforce equality. It is often promised, but rarely voluntarily given. Rather it is a continuing conquest by those who seek it."

Two roadblocks impede progress for people with disabilities, he emphasized—stereotyped attitudes and obsolete technology. He urged NIH involvement in the World Congress on Technology coming up in December in Crystal City, Va., where "scientists, educators and the disabled from all over the world will talk for the first time on the development of technology and its application in the workplace."

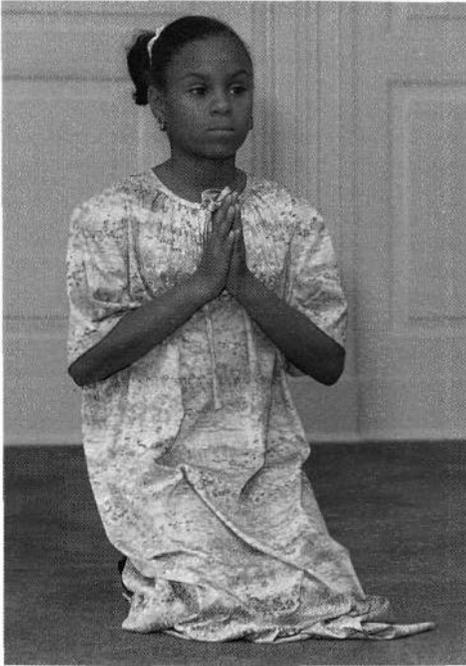
"We are going to talk about what can be done," he said. "Its central theme will be ending the (United Nations-sponsored) Decade of the Disabled and beginning the century of ability. A totally accessible society for all persons is our goal."

NEI director and NIH acting deputy director for intramural affairs Dr. Carl Kupfer, who introduced Suchanek, said, "I know it is (NIH director) Dr. Healy's goal for NIH to participate fully in the spirit of the ADA and to foster the full range of opportunities for people with disabilities."

Diane Armstrong, DEO director, presented



Members of the Performing Arts Ensemble at the Tyler D.C. Vision Program sang four songs, including "Down by the Riverside" and "America, the Beautiful," for the audience.



Stephanie Fletcher performed a dance she created to accompany the song, "Let There Be Peace."

awards to several members of the NIH advisory committee for employees with disabilities, including chairman Geller, Jerry Garmany, Dan Rogers and Denise Wray. Also recognized, in addition to Mahar and Kleinman, were NIAID's Dr. John McGowan, Charlotte Turner of the Division of Financial Management, and the *NIH Record*.

Offering songs and dances for the audience in Wilson Hall were members of the Performing Arts Ensemble at the Tyler D.C. Vision Program, who gave a moving performance.

The program's theme this year was "Work: The Key to Opportunity." Concluded DEO's Brogan, "The key is to open minds and doors, so that we can provide opportunities that millions of Americans are seeking." □

## Guide to Health Plans Offered

It's open season, and if you are confused about the many health insurance options available to you as a government employee, stop by any R&W gift shop and pick up a copy of Washington Consumers Checkbook's *Guide to Health Insurance Plans for Federal Employees*. The guide not only contains information on every government-wide, employee association, and comprehensive plan in the country, but it also attempts to answer the puzzling questions about what benefit differences mean in dollars.

The guide retails for \$6.95, but R&W members can purchase it for \$5.95, and is scheduled to be available before open season begins on Nov. 12. For more information, or to see if the guides have come in yet, call R&W, 496-4600. □

## First Science Education Awards Announced by NIH, ADAMHA

HHS secretary Dr. Louis W. Sullivan recently announced the first Science Education Partnership Awards (SEPA), which match scientists with creative educators to produce such things as videos, model curriculum materials and interactive exhibits that foster "excitement about the health sciences" in young people and the general public.

Each of the 24 funded partnerships links PHS-supported researchers or other biomedical scientists with innovative teachers, community leaders such as the Black Church Network, and media experts to produce projects that pilot teachers' institutes, a hands-on museum exhibit on the immune system and AIDS, and other programs.

Stanford University, for example, will work in partnership with Lucasfilms Learning—a multimedia design group based within George (Star Wars) Lucas' film company—to develop interactive software programs such as video discs to spark young people's interest in science on topics including the effects of drugs and alcohol.

Sullivan said, "The president has set a goal for the nation of being 'first in the world in science and math' by the year 2000. These new projects will help get us there by providing tested models in which teachers, community organizations and scientists become partners to bring the excitement of science to every child and adult in our land."

The SEPA grants, totaling nearly \$5 million, were made by NIH and the Alcohol, Drug Abuse, and Mental Health Administration and are especially targeted toward encouraging women and minorities to become interested in science.

"Because increasing scientific literacy and enhancing science education are such vital

national goals, I am looking forward to the accomplishments of these award recipients," said NIH director Dr. Bernadine Healy. "The proposals were very creative, so we have every reason to believe that the results will be innovative and impressive."

The SEPA pilot projects run the gamut of science education possibilities:

- Rutgers University—in cooperation with the Camden, N.J., school system—will provide training about modern techniques in neuroscience to all of Camden's middle school science teachers during summer training institutes.

- The American Association for the Advancement of Science, working with the Black Church Network, will develop and test a set of participatory biology activities to be disseminated to more than 500 churches for use in after-school programs, health fairs, and mall and grocery store exhibits.

- The New York Hall of Science and the Association of Science Technology Centers will develop, test and tour nationally a 500-square-foot, hands-on exhibit on AIDS and the human immune system for families, teachers and students grades 6-12.

- A rural partnership for science education in Cooperstown, N.Y.—to include a summer science training program for teachers and a summer science camp for students grades 3-8, using state-of-the-art lab equipment—will serve as a model for other rural school districts.

Nearly 200 proposals were submitted for SEPA grants, which are eligible for funding for a maximum of 3 years. Once proven successful, the 24 funded projects will be replicated for widespread use across America. □



Ground was broken on Oct. 28 for a special playground at the Children's Inn at NIH. Reviewing blueprints for the project, slated to be finished next month, are (from l) James Huckeba of Creative Leisure Products, the firm that designed and is building the playground; Clinical Center therapeutic recreation specialists Holly Parker and Rene Felder (representing the inn's board of directors), and Dave Hammett, also of Creative Leisure Products.

**BRASS***(Continued from Page 1)*

tants, and living conditions. Science is introduced when two patients come to the United States and ask the student docs to help them find out about a mysterious illness that seems to be spreading in their country. Each patient talks about symptoms and living conditions. It is now up to the docs to find out what the disease is."

During the course of the program, the students will visit the National Library of Medicine, the Biomedical Engineering and Instrumentation Program's glass unit, the clinical pathology department, genetics and environmental studies labs, and the NIH animal facility. They will also gain hands-on experience with tissue culture technology. Each Saturday, new clues will crop up as factors are ruled out via lab results. On the final Saturday morning, a mock news conference will be held where the students will present their findings. Afterward they will meet a real "sleuth" who was active in research involving the model disease.

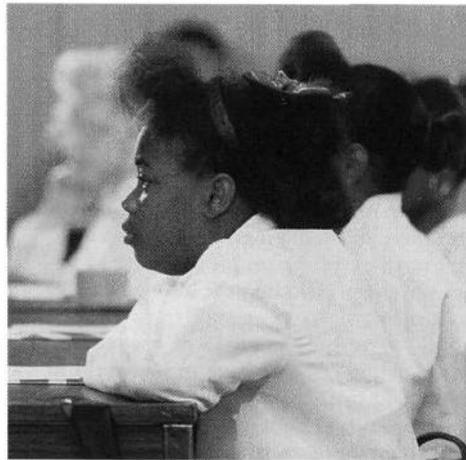
Presented with the challenge on Oct. 19, the students from Gaithersburg Intermediate School in Maryland and Browne Junior High in Washington, D.C., prepared to leave immediately to visit their fictitious country. They were given 2 hours to decide what to take on the journey. Their responses were quite good—gather medical tools that might not be available in that country and talk with other doctors to see if they had ever heard of these symptoms. To the latter response, Stempel reinforced, "That's exactly what scientists do, consult with each other." Another suggestion was to check the medical literature for evidence that the symptoms have occurred anywhere else. What better place to start than the National Library of Medicine, the world's largest medical library?

Arriving in two groups, mixed between the two schools to encourage rapport, the docs were met at NLM by members of the reference staff. Not frightened by new technology, the youngsters immediately sat down at computers and searched for related journal articles from databases on infectious and communicable diseases. After selecting some titles, they proceeded to the reading room for the actual articles. NLM's Pam Meredith explained that "Grateful Med" software was developed for doctors such as themselves and can be reached using a personal computer 24 hours-a-day. Robin Toblin of Gaithersburg was interested in figuring out how to use the computer. Several students wanted to search even further by going into the microfiche catalog files.

After the library, the group visited Bill Dehne, a glass blower for the Biomedical Engineering and Instrumentation Program of NCCR. He gave a demonstration and talked about instruments he has made during his NIH career.

"I once made an instrument designed for use in animal models to help this particular woman patient who had had three separate heart operations and always seemed to develop the same complications," he said. Benefitting from information gleaned from the animal model, the patient was later released from the hospital following a successful operation. "It made me feel good that in a small way, I had helped," Dehne said.

To prepare the students for the following Saturday's class, Stempel gave each an article



*A student listens intently as a BRASS instructor divulges details of a mysterious virus.*

about childhood communicable diseases and discussed the next week's visit to the clinical pathology department, where the docs would study what the blood test (taken from the patients earlier) reveals.

This is the first time this kind of model has been used in a federal biomedical research institution, although it has been done before in schools, said Moskowitz. "We mix detective work with library work, and offer the

kids exposure to different types of scientific investigation."

Stempel, a teacher at Poolesville Junior High School, says she deliberately included both active and passive learning in the BRASS program. "To learn a fact and then do something with it makes their retention much higher and makes learning more enjoyable. This is a new trend coming," she says.

Nick Miller, a science teacher at Charles E. Smith Jewish Day School in Rockville and collaborator for the model program, says kids may not have the best resources—library and laboratory—available to them in their home schools. "We need to make these students see that they can cope with high technology."

"The students were selected because of their interest in science," explains Stempel. "They are not necessarily the cream of the crop. After the 6 weeks are over, we need to try to hold onto them. Pull them into the system and not let them go."

Says Moskowitz, "This program is not about boosting test scores. We want it to be fun and serve as a learning experience at the same time." The rationale for choosing this age group, he explained, is that the National Science Foundation did a study confirming that career decisions are starting to be made at junior and high school levels. "Therefore, we need to provide information in order to nurture their decisionmaking.

"Much recent data shows the American public to be virtually illiterate in life sciences," continued Moskowitz. "Basic science and its applications are unfamiliar to most Americans, especially children age 12. We are facing a silent crisis with respect to two issues—science illiteracy and an anti-science attitude."

According to Moskowitz, today's high school seniors and college students are, more than ever before, choosing nonscience professions. "The pipeline is drying up. People are



*The first group of BRASS students from Gaithersburg Intermediate School and Browne Junior High School of Washington, D.C., stand in front of Bldg. 1 with their teachers, Sandi Stempel (2nd row, far r), and Nick Miller (3rd row, far r). Also with the group is Dr. Jay Moskowitz, NIH's associate director for science policy and legislation (back row, far r).*

Photos: John Crawford



Bill Dehne of BEIP's glass unit demonstrates glass blowing to the students.

not entering the medical field."

Moskowitz got involved in BRASS because he serves on the Office of Science and Technology Policy's Federal Coordinating Council for Science, Engineering and Technology. Among its goals for the year 2000 are that United States students will be first in the world in science and mathematics achievement; and every adult American will be literate and will possess the knowledge and skills necessary to compete in a global economy.

The BRASS model will be evaluated during this fall session and again in the spring, when two new schools will be brought in from Fairfax and Prince George's counties. "If it is a success," says Moskowitz, "we will package the curriculum and provide it to other institutions, both federal and grantee, across the country."

Judging by the students' reaction, BRASS is on its way. Several students joined

Gaithersburg's Ken Duffy in describing their first Saturday morning as "fun and challenging." For many, it was their first visit to NIH and the world of research. Each formed their own opinions. While Lemir Starks of Gaithersburg said he would not like to be a glass blower, Hardy Wister from Browne liked the glass blowing unit the best.

"We need you," Moskowitz told the group, after thanking them for giving up their Saturday mornings to participate in the BRASS program.

"We need another generation of scientists, physicians, researchers, technicians, nurses, social workers, animal workers, and science teachers. We want you to become literate not only so you can make informed decisions about your own health, we also want you to experience the excitement of research, learn how we unravel mysteries about ourselves, and become ambassadors for biomedical science and NIH." □

## Health Benefits Fair Planned

In conjunction with the 1991 Federal Employees Health Benefits Program open season, which runs from Tuesday, Nov. 12 through Monday, Dec. 9, the Recruitment and Employee Benefits Branch, Division of Personnel Management is sponsoring a Health Benefits Fair. The fair will be held in Bldg. 1, Wilson Hall, on Tuesday, Nov. 19, from 10 a.m. to 2 p.m. Representatives from most of the plans that are available to NIH employees will be on hand to answer questions on 1992 benefits. The NIH advisory committee for employees with disabilities will also be there to assist employees who need help getting information. □

## Female Volunteers Sought

Women with regular menstrual cycles, ages 18-40, are needed to participate in a study of the effects of nutrition on the menstrual cycle. Volunteers must know the usual duration and frequency of their menstrual cycle, should not be on the birth control pill, should have stable weight and eating habits, and must be willing to spend 7 nights and 6 days as an inpatient at the Clinical Center. Some individuals will be randomized to a 3-day fast; volunteers must be willing to not have food by mouth for 3 days. Subjects will be paid; those who fast will earn more. Call 496-4244 and leave message. □

## Sunscreen Prevents Fever Blisters, Scientists Show

Application of a sunscreen can prevent recurrence of fever blisters (herpes labialis) that are induced by exposure to ultraviolet light, a natural component of sunlight, Dr. James F. Rooney reported at the 31st Interscience Conference on Antimicrobial Agents and Chemotherapy (ICAAC), sponsored by the American Society of Microbiology.

"Routine use of sunscreen by people with a history of oral herpes would be a simple, cost-effective approach to reduce the estimated 25 million episodes of sun-induced recurrent fever blisters that develop each year," said Rooney, of the Laboratory of Oral Medicine, NIDR.

Fever blisters, or cold sores, are caused by herpes simplex virus type 1. "Although the majority of infections are mild, patients frequently express concern about the symptoms, the appearance of the sores, and the possibility of transmitting the virus to others," he said.

After the first oral herpes infection, usually in childhood, the virus remains dormant in a nerve near the cheekbone. The virus may stay inactive permanently or may be periodically reactivated, traveling down the nerve to the skin surface where it causes recurrence of fever blisters. Sunlight, specifically the ultraviolet B (UVB) component that is most responsible for sunburn, is one factor that triggers reactivation of oral herpes, Rooney explained.

Rooney and his colleagues exposed 38 patients on two separate occasions to UVB light equivalent to 80 minutes of midday, midsummer sun (enough to cause a mild sunburn) on an area on the lips where fever blisters had previously appeared. Before each exposure, a solution containing either sunscreen or an inactive solution (placebo) was applied to the lips. Each patient received, in random order, one exposure with sunblocker and one with placebo.

In the placebo group, 27 of 38 persons (71 percent) developed a fever blister within 1 week of UVB exposure. In contrast, when a sunscreen was used, none of the patients had a recurrent herpes sore.

"UV light is a potent stimulus for reactivating oral herpes, but application of sunscreen may provide an effective means of preventing sunlight-induced recurrent infections," Rooney concluded.

In addition to Rooney, the research group included NIDR colleagues Dr. Abner Notkins, Margaret Mannix, Charlyce Wallington and Charles Wohlenberg; Drs. Stephen Straus and Steven Banks of NIAID; and Dr. Yvonne Bryson and Maryanne Dillon at the University of California, Los Angeles.—  
Patricia Sheridan □

*Seven-Year Effort***Watsons Earn Black Belts in Martial Art**

By Rich McManus

They are probably the last couple at NIH with whom you'd care to engage in a scuffle. And they are probably the least likely to become involved in such unpleasantness. John and Diane Watson are simply committed athletes who recently earned their first-degree black belts in the Korean martial art known as tae kwon do.

Seven years ago, the two, who are now in their fifties, were casting about for a form of exercise that both could enjoy together. They already had tennis, biking and skiing in common and, at that time, Diane was playing on a county-league women's soccer team coached by John.

"We considered weight training for a while, but basically we were looking for physical activity that we could do together," recalls Diane.

Says John, "Diane and I like to balance physical activity with work and our spiritual lives."

It turned out that what both were seeking was right in their own back yard. Not only is the Thomas E. Malone Judo and Tae Kwon Do Center conveniently located in the basement of Bldg. 31, but also its volunteer teaching staff includes fifth-degree black belt W. French Anderson, an international master instructor with more than two decades of tae kwon do expertise. He founded the NIH Tae Kwon Do Club in 1978 and heads it still.

The Watsons saw an ad for martial arts in the *NIH Record* and decided to give it a try.

"The article announcing the group said the club was supposed to teach self-defense to professionals. And having it close by at Stone Ridge (where classes were held prior to construction of the Malone Center) was a real big boon to us."

Diane, the grants management officer at NIAMS, was an utter rookie in martial arts. She picked tae kwon do first because of convenience and second because it combines learning with physical exercise.

"I never anticipated getting to this point," she said a few days before earning her black belt—the tenth stage she has reached, starting with a white belt.

Why continue with an art that demands so much time and concentration, not to mention changes of clothing as one progresses from white to gold to green to blue to red to black belts (not counting intervals where all you earn is a colored stripe)?

"There are many things I like about tae kwon do," Diane begins. "It's healthy. All the movements give you muscle tone and strengthen your body (quite believable because, at age 50, she looks a decade younger). It's a discipline involving routine and concentration. You have to like repetition. You have to let your mental reflexes control your body."

Tae kwon do is not a sport, says John, who is chief of NHLBI's Devices and Technology Branch.

"As it is practiced at NIH, it's really not a



Diane Watson, the grants management officer at NIAMS, performs a front kick with punch during her black belt exam. Photos: Ernie Branson

sport, but a martial art," he says. "In sports, you may go out and compete in regional events and contests. Everything we do (in tae kwon do) is for the mutual benefit of the club members. It's a supportive, as opposed to a competitive, environment."

Both Watsons claim that the benefits of tae kwon do extend into their working lives.

"I've got more focus," says Diane, who also reports her balance has "improved tremendously. You learn to think before you act, and how to breathe more effectively. It also improves my sense of centeredness, or what is called 'ki.'"

Offers John, "It helps you focus your attention on priorities, and set them. It makes it easier to handle difficult tasks. Physically, you feel good. It really helps you with your job."

"The neat thing about tae kwon do is that you're always learning," Diane adds. "You're always experiencing a higher level of awareness about your surroundings. You learn about yourself, your behavior, and how to respond in different situations. And much of what you learn can be translated to the workplace. You learn not to be distracted, to go with the flow."

Only once since they took up the defensive art of tae kwon do have the Watsons found themselves in a potentially threatening situation.

"We were in southern Maryland at a fast-food place when a domestic squabble broke out," recalls John. "A guy pulled out a big knife. My reaction was to be ready. I made a decision about what I would do if attacked. But nothing came of it and the situation quieted down."

You never assume a threatening posture or tip your hand about what you might do if attacked, he emphasized. The real essential is assessing the situation properly and practicing prevention.

The club meets four times a week, but the



The jury for the Watsons' exam included (from l) Dr. Donald Murphy, Dr. Art Boujoukas, Dr. Daniel Eskinazi, Dr. W. French Anderson, and Dr. Jean Grem, all of whom are black belts in tae kwon do.

Watsons can usually attend only two or three. They particularly enjoy Friday night sparring sessions.

"French is usually there and it's kind of a nice way to end the week, to get the cobwebs out," said John.

Classes start slowly as members, barefoot and wearing their white uniforms or "dobuk," spend the first half-hour practicing fundamentals—punches, blocks and kicks.

"It's sort of like aerobic exercise," says John.

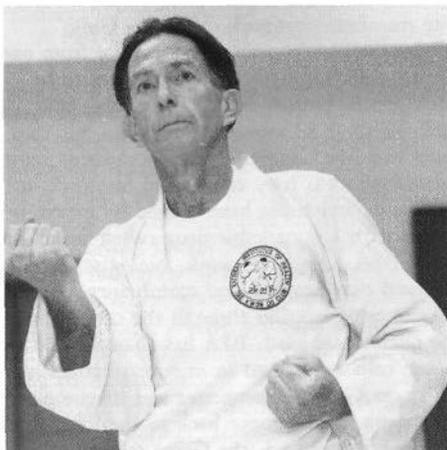
For the next half-hour members practice "forms," which are basic defensive movements choreographed as though one were meeting attacks from one to two opponents.

"You improve your technique from this," says John, "and improve balance, mental concentration, and focus. You never do one of these forms perfectly. You can always be more relaxed, more powerful, more precise, more focused, and use more economy of motion."

Club teachers, who include third-degree black belt Don Murphy and second-degree black belts Jean Grem and Daniel Eskinazi, critique the students as they practice forms, also known as "hyung." Crucial to each move is that students make use of inertia and momentum.

"That's how a little thin guy can demonstrate a lot of power—you learn to use momentum and mass in a more effective way," said John, who is thin but not especially little. "The more you learn, the less you want to use it. It's always better to avoid a threatening situation."

Deeply involved in careers, the Watsons appreciate the flexibility of their art: "The nice thing about it is that you don't need a special room, or equipment, or another person to practice," says John. "Though I'm very fortunate that Diane likes it, too."



Dr. John Watson, chief of NHLBI's Devices and Technology Branch, demonstrates a block; he and his wife earned black belts in tae kwon do 7 years after joining NIH's Tae Kwon Do Club, which meets at the Thomas E. Malone Judo and Tae Kwon Do Center in the basement of Bldg. 31.



Part of the exam included sparring. Here Diane blocks a kick by husband John as French Anderson looks on. A small gathering of family and friends watched the Watsons pass their black belt exam.

Sometimes the two practice at home, each teaching the other.

"What's unique about the club is that all the teachers are volunteers," John explained. Their black belts in hand, the Watsons will on occasion be assistant instructors in the club.

"We like the environment," he says. "It's very supportive. We've learned and benefitted from working with each of our fellow club members. There's no competition, either between my wife and I, or in the club."

Interestingly, progression within the club is not a matter of a student's choosing. Rather, members are invited to test for higher belts when their instructors feel they are ready.

"It has been a long, hard, difficult road for me," admitted Diane on the eve of her black belt exam, when she had to execute 10 forms, each progressively more difficult. She is the first woman at NIH, and John is the second male, to go from a beginner through all stages of advancement to a black belt in the club's history.

"You have to be persistent, a plodder, someone who plugs away," she said. "You have to know that your ship will come in some day, although you're not exactly sure how, or where, or when, or why."

A wooden board that she split with her fist adorns one wall of her office, offering testimony to her tenacity—and power.

"They say the real improvement comes after you get your black belt," said the Watsons. "Getting the belt is not really the end, but the beginning."

"They did fine," reported examiner Don Murphy after the test, which was attended by friends and family. "They did a good job. We're pleased with them."

There are 10 ranks within the black belt, he explained. "Ranks 9 and 10 are extremely rare. And degrees 5 through 7 often reflect major leadership activities."

Both Watsons intend to keep learning and practicing.

"It really has been fun for John and me to do it together and share the experience," says Diane. "Fortunately we both like the physical aspects of working out."

Asked whether her art involves adopting any sort of Eastern philosophy, she answers, "You get it in dribs and drabs. Basically, we're there to learn from each other, and to learn about ourselves. Don's always reminding us that we need to take care of each other, that we're partners. He calls the gym a 'dojo' or 'place of enlightenment,' and I guess that's truly what it is."

"Some experiences are not always pleasant," she confided, "like not being advanced a degree." And yes, she has felt like quitting: "Yeah, yesterday," she laughs.

But quitting is not on her horizon. Not until she learns to develop "a pretty, powerful side kick."

Anyone interested in obtaining information about the club should contact Dr. Don Murphy, 496-1736. □

### Inn Fundraiser Needs Help

As part of a holiday fundraising effort for the Children's Inn at NIH, White Flint Mall and radio station WLTT-97.4 FM will be holding a promotion from Nov. 22 to Dec. 22 at the mall. To volunteer or get more information, contact Claire Cardella, 652-1227, or Randy Schools at R&W, 496-6061. □

### Wanted: Carpool Members

An existing carpool from Gaithersburg to NIH would like one or two more members to share in driving. Work hours are 8:30 a.m. to 5 p.m. Call Judy Jaworek, 496-3251, or Judy Steckel, 402-0026. □

## NICHD Scientist Richard Klausner Widely Honored

By Birgit An der Lan

This year, Dr. Richard Klausner, chief of NICHD's Cell Biology and Metabolism Branch, has been honored by several institutions around the country for his seminal contributions to cell biology and biochemistry. In April he delivered the Abelson Lecture at Washington University in St. Louis, and in May the Institute for Clinical Research in Medicine bestowed on him the Marcel Piché Award at its annual meeting in Montreal. In May he also delivered the Kroc Lecture at Harvard. In October he delivered the three Lampton Lectures at Columbia, entitled "Building a Multi-Subunit Signalling Complex," "A New Model for Regulation of Membrane Traffic and Organogenesis" and "Regulating Metabolic Pathways after Transcription: Lessons from Human Iron Metabolism." Each lecture summarized the advances he has made in three separate areas of biology. In November he will give the Fagan Memorial Lecture at Stanford as well as the Shannon Lecture at Harvard. The Shannon Lecture is given in memory of Dr. James Shannon, NIH director during the period of its most rapid growth. Previous lecturers include such luminaries as Dr. Francis Collins, discoverer of the gene for cystic fibrosis.

Klausner spent his undergraduate years at Yale, earned his M.D. from Duke University Medical School, and trained in internal medicine at the Massachusetts General Hospital. He came to NIH in 1979, and since his appointment as chief of the Cell Biology and Metabolism Branch when it was founded in 1984, his research has taken three major directions.

### Signalling Across the Cell Membrane

All cells, be they simple bacteria or the more complex building blocks of higher organisms, live in an ever-changing environment, to which they must adapt. Cells have evolved complex mechanisms to transmit external signals across the cell membrane to the cell interior, and for the last two decades biochemists the world over have been trying to unravel the secrets of this relaying process.

Klausner and his colleagues have been studying the most complex of these signalling mechanisms yet discovered: the process by which the T lymphocytes recognize cells, such as macrophages and B cells, that have been invaded by pathogens, and by which they orchestrate the response of the immune system. T cells thus serve as the sentinels of the immune system, and to enable them to carry out this function they have a special receptor on their surface, which can sense and ensnare cells harboring pathogens. These sensing devices are called T cell antigen receptors or TCRs.

Klausner's work has had a major impact on



Dr. Richard Klausner

this field of research, clarifying both the structure and the function of the TCR. This receptor consists of three groups of proteins, which span the cell membrane of the T cell. Klausner's lab was the first to identify a previously unknown group of these proteins (called the zeta group), and to determine how the whole complex of these proteins is assembled. This was accomplished with one of the most powerful techniques of modern biology—making subtle alterations in the gene encoding the protein of interest, and observing the biological effects of introducing this mutated gene into cells that carry a disabled form of the gene, a technique known as mutation and transfection.

The reason this receptor is exceptionally complex (it has eight components, whereas most other receptors consist of a single protein embedded within the cell membrane) is undoubtedly that the T cell has many different functions. For example, when it encounters a pathogenic antigen, it divides rapidly and releases growth factors such as interleukin 2 that promote this cell proliferation. Klausner's group proposed that different parts of the TCR are linked to different intracellular processes. Mutation and transfection experiments have helped the group explore the roles of each of the TCR components once the receptor becomes engaged, work that has led to the identification of specific amino acid sequences within the subunits that directly couple the receptor to various metabolic pathways within the T cell.

### Cellular Traffic in Molecules and Membranes

Studying the assembly of TCR subunits led Klausner into another field of biology, research that in his hands has proved to be extremely productive, and has had a significant impact on the way cell biologists think about movement of materials through the cell.

Surface components such as the TCR are synthesized and assembled within the T cell in the so-called endoplasmic reticulum, or ER, an elaborate interconnected membrane network of canals and lagoons. Again using the techniques of mutant selection and transfection of appropriate genes, Klausner's lab has established the order in which the components of the TCR are assembled and has tracked the individual subunits of the TCR as they move through the cell's membrane system to their final destination on the T cell surface.

It has become clear from this work that only fully assembled TCR complexes can be integrated into the cell surface membrane; those lacking any one of the component parts are rapidly destroyed within the cell. Klausner believes that this guards against a scenario where the immune response is blocked because the occupied receptors are incomplete and thus unable to couple with intracellular processes.

These observations have led Klausner to the discovery of what he calls "architectural editing," a type of cellular quality control. This quality control depends on the waste disposal machinery of the cell recognizing certain amino acid sequences that remain exposed until the complete TCR is assembled. These amino acid sequences act as molecular signals for retention and degradation unless they are masked during TCR assembly. The TCR subunit that Klausner and his colleagues discovered, the zeta subunit, seems to have a critical role in this masking process.

One of Klausner's more recent research interests has been how membrane traffic within the cell is regulated. Proteins destined for secretion or for incorporation into the surface membrane of the cell are first transferred from the ribosomes, where they are made, into the internal space of the ER, where they undergo an initial processing. From here they are sent to a further processing plant, a separate membrane network called the Golgi apparatus. For the protein to traverse from one membrane system to the other, it has to be packaged in a small membrane bubble that buds off the ER, moves through the cell, and fuses with the Golgi. Some of Klausner's most innovative ideas have come from his work in this field, which has been helped by experiments with a remarkable drug called brefeldin A, or BFA. Until this work, biologists believed that proteins and membranes moved only in one direction through the cell—from the nucleus outward. BFA has changed that. When cells are bathed in minute amounts of BFA, the Golgi disintegrates and its component parts rapidly move back to the ER; after the drug is removed, the Golgi reforms (the first observed example of a cell organelle forming from scratch).

Klausner has proposed that in normal cells there is a constant back and forth between these two membrane systems, and because the forward movement normally predominates, the

backward movement was never detected. BFA causes disintegration of the Golgi because the forward movement is disrupted. Klausner and his coworkers have shown that BFA prevents ER membrane bubbles from fusing with the Golgi because it interferes with the binding of a specific fusion-promoting protein—and by doing so upsets the normal balance of inflow and output of membrane material. BFA is also proving to be an invaluable tool to probe the molecular details of this critical cell process.

#### Switching on Genes with Iron

Klausner is also known as a pioneer in the field of regulation of gene expression at the level of messenger RNA (rather than at the level of gene transcription). He and his colleagues were the first to propose a mechanism for this type of post-transcriptional control in higher animals. The paradigm for this research has been a pair of proteins responsible for regulating iron levels in the cell: the transferrin receptor, which transports iron into cells, and ferritin, which mops up excess iron within the cells. A steady iron level within the cell is critical to its survival—too much iron is toxic, too little iron prevents cell growth and division.

In the course of these studies, the iron responsive element (called "IRE") was discovered, a hairpin-like loop in the messenger RNAs of both proteins that makes their translation sensitive to iron. The group then went on to identify a protein that binds to the IRE in an iron-dependent manner—the IRE bind-

ing protein, or IRE-BP. The binding protein sticks to the IRE when iron is scarce, acting like a road block to translation in the case of ferritin, and preventing degrading enzymes from destroying the messenger RNA for the transferrin receptor. Interfering with translation of ferritin messenger RNA and stabilizing transferrin receptor messenger RNA has the net effect of making more iron available to the cell.

Recently Klausner's group sequenced the IRE-BP, which has enabled the researchers to determine how it can sense iron levels. The active site of the molecule is a cleft containing sulfhydryl groups. When iron interacts with these groups, the IRE-BP is drawn into a tighter configuration, which is unable to bind to the messenger RNAs; by contrast, when iron levels are low, the IRE-BP assumes a looser form that can drape itself around the IREs in the messenger RNAs.

Once scientists have the sequence of a protein, they can compare it with those of others, such comparisons often yielding surprising results. The sequence of the IRE-BP, particularly of its active site, bears a striking resemblance to that of a mitochondrial iron-dependent enzyme called aconitase. Aconitase was discovered in the thirties, and its structure is well characterized, which is helping Klausner's group to deepen its insights into the workings of the IRE-BP. As the first example of post-transcriptional gene control to be worked out in such detail, this body of research is having a profound influence on the field. □

#### Maronpot Heads NIEHS Branch

Dr. Robert R. Maronpot has been named chief of NIEHS's Experimental Toxicology Branch. Before this appointment, he headed cancer genetics and molecular pathology in the institute's Experimental Carcinogenesis and Mutagenesis Branch.

The branch provides data to support the characterization of toxicological properties of important consumer, industrial, and environmental chemicals. Located within the Division



Dr. Robert Maronpot

#### Panniers To Head Study Section

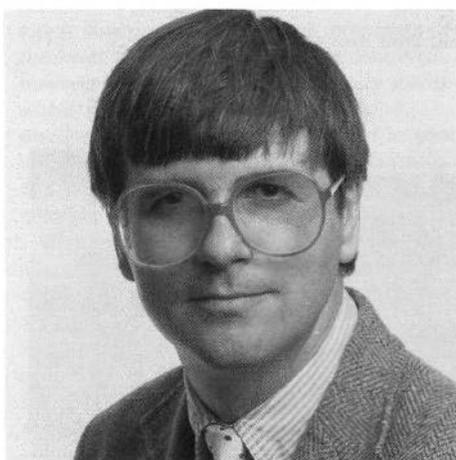
Dr. Richard Panniers, assistant professor of oncology and biochemistry, University of Rochester, has been appointed scientific review administrator in the Division of Research Grants.

A native of Wales, he will be responsible for the management of special study section Z, one of 101 review groups in DRG's Referral and Review Branch. These groups provide the first level of NIH's peer review system for awarding research and training grants.

A former grantee principal investigator, Panniers has received research support from the American Cancer Society and the Life and Health Insurance Medical Research Fund. He has an extensive research background in cellular physiology, protein purification and enzymology of mammalian protein synthesis and its regulation.

He received his B.Sc. with honors from University College, London in 1976, and his Ph.D. in biochemistry from St. Georges Medical School, London, in 1980. While at University College he was winner of the Plimmer Prize in biochemistry in 1975.

Panniers came to the United States in 1980 as a research associate at the University of Rochester's cancer center. In 1983, he was



Dr. Richard Panniers

senior instructor of oncology and in 1986, he became assistant professor of oncology.

He is currently a referee for *Biochemical Journal* and *European Journal of Biochemistry*. He is author of 16 articles and has made numerous presentations at major scientific meetings. He is a member of the American Society of Biochemistry and Molecular Biology and the American Association for the Advancement of Science.

of Toxicology Research and Testing, the branch also supports NIEHS efforts within the National Toxicology Program.

A native of Boston, Maronpot attended Michigan State University where he received his B.S., D.V.M., and M.S. degrees. He received his M.P.H. degree from Harvard University.

He is a member of the board of directors of the American Board of Toxicology, and serves as an adjunct professor in the department of microbiology, pathology, and parasitology in the College of Veterinary Medicine at North Carolina State University. Before joining NIEHS in 1981, Maronpot was a senior fellow at Carnegie-Mellon University.

He is a diplomate of the American College of Veterinary Pathologists and of the American Board of Toxicology. He has published more than 120 articles in the scientific literature as well as a number of book chapters, and he serves on the editorial boards of five scientific publications.

In off-duty hours, Maronpot is also a gifted photographer and has received a number of awards for his pictures. □

## NIH Fire Department Demonstrates Its Expertise

The NIH Fire Department, part of the fire and emergency response section, Emergency Management Branch, hosted a recent meeting of the federal fire service task group as part of its Fire Prevention Week activities. Composed of federal facilities fire chiefs and program managers nationwide, the task group has a mission to further fire protection and safety initiatives in federal installations.

Following a formal meeting at the Stone House, the group moved outside to watch a hazardous materials control exercise put on by the NIH Fire Department. The scenario, planned to reflect the type of incident and materials used at NIH, consisted of a 55-gallon drum of acid rupturing and leaking into the rear of a cargo truck. NIH Fire Department personnel arrived on the scene, evaluated the situation, initiated safety procedures, confined the spill, donned the necessary protective equipment readying themselves to enter the spill site and then plugged the drum. After controlling the leak, fire fighters demonstrated the proper procedure for decontaminating personnel and equipment exposed to the acid.

Following the hazardous materials demonstration, an emergency response and fire protection equipment demonstration was held for the task group.

Photos: Ernie Branson



NIH fire fighters don self-contained breathing apparatus in preparation for dressing out in chemical-resistant entry suits.



The NIH Fire Department recently placed in service a new hazardous materials response vehicle. This vehicle was designed by the fire fighters specifically for the emergency response needs of NIH. The fire department receives more than 1,700 emergency calls for assistance each year including more than 350 chemical, biological and radioactive materials incidents.



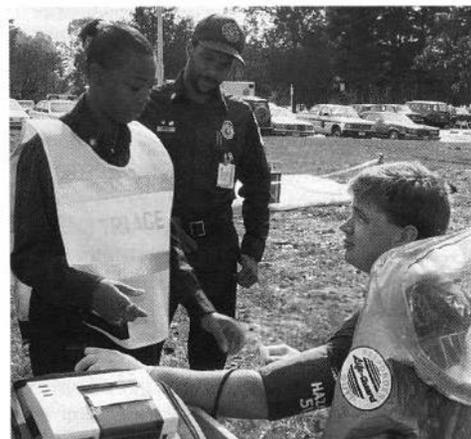
The primary entry team has set up containment around the vehicle and suppressed the flow of acid.



Decontamination consists of several stations coinciding with the degree of hazard. In photo, fire fighters wait at their assigned stations to carry out the necessary procedures.



The fire department safety officer, haz-mat officer and entry teams discuss mitigation procedures to ensure a safe operation.



Triage/EMS personnel monitor the vital signs of entry team members. Prior to and after each entry into the contaminated zone, blood pressures, pulse rates, respirations, and temperatures are monitored and recorded to ensure that no ill effects were experienced by the entry team members.

## Magnetic Resonance Imaging Techniques Prove Faster, More Powerful Than Ever

By Charlotte Armstrong

The information scientists glean from spinning atomic nuclei is providing an ever-more-powerful means of viewing the body's interior contours and monitoring its chemistry, according to speakers at NIH's recent science writers seminar on magnetic resonance imaging (MRI).

Scientists from NIH's state-of-the-art In Vivo NMR Research Center gave an overview of studies under way here and at other centers that are aimed at exploiting and expanding MRI's applications as a clinical diagnostic and research tool. (NMR, or nuclear magnetic resonance, is the original term for this technology.)

Dr. Edwin Becker, chief of the nuclear magnetic resonance section, Laboratory of Chemical Physics, NIDDK, opened the seminar with an overview of the physical basis of MRI and its capabilities.

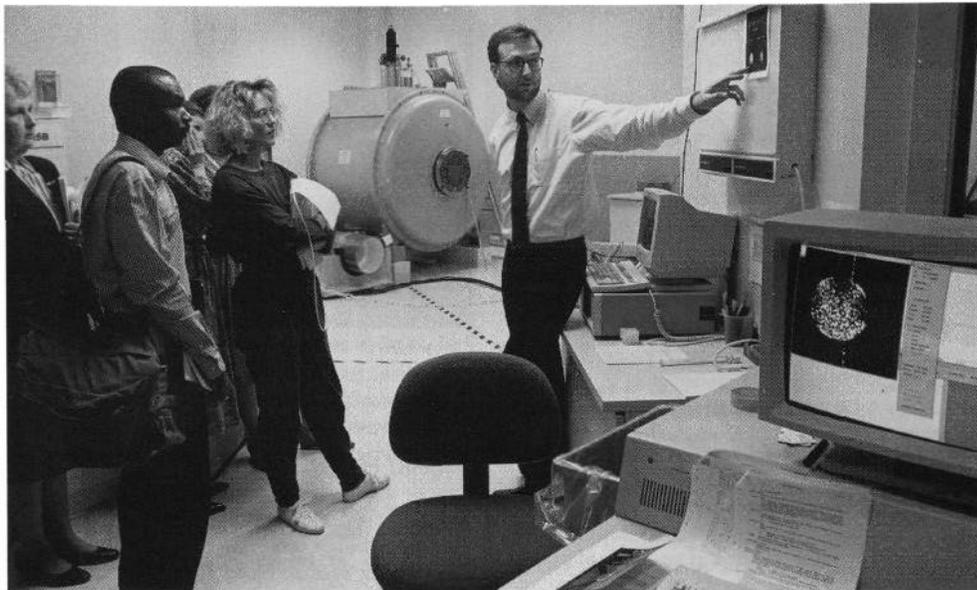
MRI uses the magnetic properties of atomic nuclei to obtain chemical information on solutions and tissues and to generate cross-sectional images. MRI involves no ionizing radiation and can be done noninvasively. The ability to do scans harmlessly in living organisms has implications for both the safety and quality of information gathering.

MRI makes use of the fact that the nucleus of an atom, which has a positive charge, spins, thereby creating a small magnet. When these nuclear magnets are exposed to a uniform external magnetic field, they align themselves like tiny bar magnets. A pulse of electromagnetic energy is applied to tip them out of alignment. The frequency applied to make this tip is very close to a characteristic frequency of the nucleus itself, hence the term nuclear magnetic resonance.

Before the nuclear magnets return to alignment with the external magnetic field, they induce an electrical signal in a coil placed around a subject in an MRI device. The chemical environment of the nuclei affects the characteristics of this signal and provides information on the composition and concentration of the tissues being studied.

Because resonance frequency is characteristic for each element, scientists can select the nuclei they wish to study with MRI. Water is abundant in living tissues, so MRI studies often focus on the hydrogen nuclei in water.

In the 1970's scientists discovered that when sample tissue is exposed to an additional magnetic field gradient (i.e., a magnetic field that is stronger on one side than the other), the frequencies of the resulting signals reflect the location of the nuclei being detected. Scientists can select how data are collected in an MRI scan depending on whether they want, for example, visual contrast between tissues or to provide information on metabolism and



*Dr. James Pekar (r) an NIAAA senior staff fellow, interprets an MRI scan for attendees of the recent science writers seminar on MRI during a tour of the NIH In Vivo NMR Research Center. At rear is a 4.7-tesla magnet used for research studies.*

physiology.

Dr. Chrit Moonen, manager of NIH's In Vivo NMR Research Center, administered by NCRR, described the versatility of MRI scanning in studying function as opposed to anatomy. MRI can be used to study macroscopic function *in vivo* such as movement of the heart and joints. Moonen concentrated, however, on MRI's capacity to study microscopic functions by imaging specific metabolites in living tissue involved in processes like cellular energy turnover, amino acid and neurotransmitter metabolism, and osmotic pressure regulation.

Magnetic resonance spectroscopic imaging can now provide a picture of how the concentration of a selected metabolite varies across a particular slice of internal tissue. Similar information on several different compounds can be gathered simultaneously. In addition, transport functions like flow, perfusion and diffusion can be measured by MRI. Scientists can now obtain pictures of movement—such as three-dimensional images of blood vessel flow, capillary perfusion, and the diffusion of water.

NIH scientists are refining MRI's ability to visualize local differences in diffusion. Using animals models of stroke, they have found that the degree of local diffusion is changed in the area affected by stroke. While this research is preliminary, these studies suggest that MRI could be used to determine the stage of a stroke very early in its course, while it may still be possible to reverse the damage.

New techniques for speeding the generation of images are helping make possible some of the MRI functional studies described above. Dr. Robert Turner, a visiting scientist with the Laboratory of Cardiac Energetics, NHLBI, described research under way on methods that reduce the time required for a single scan from minutes to a fraction of a second. Since multiple scans are required for each study, this would also decrease the time subjects have to remain in the tight confines of the magnet—a problem for some patients—and thereby reduce cost because more scans could be done per machine.

Conventional MRI scans are time-consuming because, in making a two-dimensional image, the device samples the signals as magnetic field gradients are applied in individual linear sweeps, one sweep after each radiofrequency pulse tips the protons out of magnetic alignment. In the echo-planar imaging (EPI) technology discussed by Turner, the machine switches magnetic field gradients very quickly while data are continuously sampled, in order to gather all the data needed for a cross-sectional image after only one radiofrequency pulse tips the protons being scanned out of magnetic alignment.

This is a significant technical challenge, but the speed EPI offers makes it possible to do complete scans of a patient in 10 to 12 minutes as opposed to 1 or 2 hours. The technique also makes possible studies that require rapid repeated scanning, without the

**(Continued on Page 14)**

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visual artifacts created by motion in conventional imagers. EPI is ideal for following the movement or pulsing of joints and internal organs. The quality of EPI scans is high, and in some cases similar images would be difficult or impossible to get with any other technology.

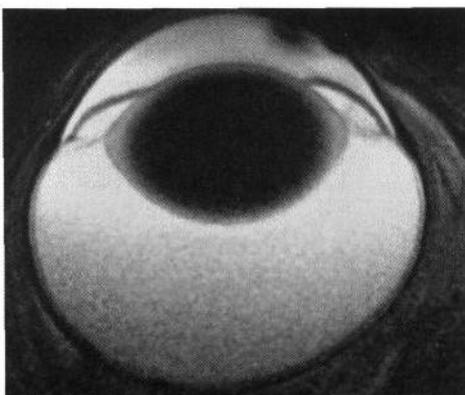
The passage of contrast material, monitored with "snap-shot" scans taken in rapid sequence, can reveal changes in blood volume and perfusion that reflect tumor growth or loss of circulation from stroke or heart attack. For example, blood perfusion at the edges of a tumor—where it is growing—is high. EPI could be used to monitor growth of a brain tumor and the effects of treatment. Similarly, MRI scans with contrast material can reveal the areas of cardiac muscle starved of blood after a heart attack.

In studies in monkeys done by Turner and his colleagues, EPI scanning of the passage of contrast material has made it possible to produce maps of blood volume in the brain. Such images could delineate the area of the brain being stimulated as it happens, suggesting the possibility of detailed research on the brain's functional architecture.

The speed of EPI is also critical to studies of water diffusion in tissues. Study of diffusion is difficult with conventional MRI because of artifacts caused by motion. However, EPI can detect abnormalities in diffusion in brain tissue. Changes in diffusion in the grey matter of patients with Alzheimer's disease, for example, may reflect the tissue's loss of organization in this disease. EPI might one day be used for the noninvasive diagnosis of Alzheimer's disease.

NIH is one of four centers in the world with the hardware necessary for EPI. "Add-on" components that can be used in conjunction with existing conventional hardware to provide EPI imaging capability are already being marketed, and Turner predicts that commercial EPI imagers may be available in 2 years.

The use of MRS (magnetic resonance spectroscopy) to study metabolites in living tissue has redirected and opened up new areas of research in physiology. Dr. Robert Balaban, chief of NHLBI's Laboratory of Cardiac Energetics, described how his MRS studies of phosphate in cardiac muscle overturned the traditional picture of energy exchange in muscle. Conventional theory held that the rate of production of adenosine triphosphate (ATP), a molecule in which energy from food is stored for cellular use, depends on the concentration of two molecules from which ATP is generated, adenosine diphosphate and inorganic phosphate. MRS studies at NIH of phosphate turnover in the heart in animals undergoing stress testing showed that, in fact, concentrations of these three molecules are quite



*The detail in this high-resolution image of an in vivo rabbit eye demonstrates the potential of MRI in the evaluation of numerous eye disorders including diabetes and retinal defects.*

constant, even with a fivefold increase in exercise level. While such insights are important scientifically, they may also provide the basis for a much more sensitive means of testing whether cardiac blood flow is adequate to support muscle contraction.

MRS studies of kidney metabolism revealed in an unexpected way a fundamental and previously unknown means by which the kidney maintains osmotic balance, that is, the fluid balance across membranes. Balaban and coworkers discovered the presence of until-then unidentified compounds in the kidney in high concentrations. Ultimately, these were found to be responsible for up to 50 percent of the kidney's osmotic balance. They play a key role in protecting cells in the kidney from the potentially toxic effects of the high concentrations of urea and sodium that are necessary for the formation of urine.

The notion that organic compounds, rather than inorganic ions, played an important role in osmotic balance has opened up a new field of investigation. The knowledge of kidney function and dysfunction that is emerging from these studies should contribute to an understanding of kidney disease.

Finally, Balaban described how physiologists are developing ways to better exploit the interaction of water protons with specific macromolecules to provide better contrast between tissues. This has been especially useful in various diseases since the concentration and composition of macromolecules are considerably different in diseased than in healthy tissue.

Macromolecules such as lipids, connective tissues and various proteins influence the MRI signal of water and therefore can be used to generate image contrast. Using this principle, scientists at the University of Pennsylvania have been able to follow the early progress of multiple sclerosis by using this technique to identify areas where the lipid sphingomyelin, a compound that is an important component of the sheathing around nerves, is deteriorat-

ing. Other imaging techniques failed to reveal these changes.

A tour following the seminar took participants through NIH's In Vivo NMR Research Center and included a stop at the center's 4-tesla, 1-meter-bore magnet contributed by NHLBI. (A tesla is a unit for magnetic field strength. The field of this magnet is about 80,000 times greater than the Earth's magnetic field.) Studies at NIH using these powerful magnets promise to further expand the already formidable capabilities of MRI imaging. □

### **Women's Health Studies Aided**

NIH recently awarded more than \$816,000 to scientific investigators across the country to expand high-priority research on women's health and to increase the number of women, including minority women, in such studies. These funds are supplements to existing research grants.

"These important supplements will not only enhance the recruitment of women into ongoing studies," said NIH director Dr. Bernadine Healy, "but will also help scientists develop innovative techniques to recruit women into future studies. The supplements demonstrate the commitment of the NIH to women's health research, and can help us learn how to better design and administer research protocols to meet women's needs."

Half of the principal investigators receiving these awards are women.

The 20 one-time supplements represent the first funds awarded by the 14-month-old NIH Office of Research on Women's Health. The awards support basic biomedical studies, large community health projects, and disease research in areas including breast cancer, heart disease, AIDS, sexually transmitted diseases, arthritis, interstitial cystitis, hearing loss, dental disease, incontinence, and a number of issues related to aging. The studies represent research that will benefit women across all stages of the life span. For instance, one study is investigating the relationship between human papillomavirus infection and cervical cancer, and another is examining the differences between men and women in graft success after coronary bypass surgery.

Healy stressed that "these supplements are only the beginning, and are part of the long-range plan to increase attention paid to research on women's health throughout the various institutes, centers and divisions of the NIH, and to improve the health of women everywhere."

The Office of Research on Women's Health was established in September 1990 to assure that research conducted and supported by NIH adequately addresses issues regarding women's health, and to assure appropriate participation of women in biomedical research. These supplemental grants are one of the new initiatives implemented by ORWH. □



## TRAINING TIPS

The NIH Training Center of the Division of Personnel Management offers the following:

<i>Courses and Programs</i>	<i>Starting Dates</i>
<i>Management and Supervisory 496-6371</i>	
Efficient Reading for Professionals	11/26
Effective Presentation Skills	12/16
Meetings That Get Results	11/18
How To Write and Publish Scientific Papers	11/20
<i>Office Operations and Administrative Systems Training 496-6211</i>	
Telephone Communication	12/11
Federal Supply Schedules	12/6
Filing and Maintenance	12/13
Quality Writing I	12/6
NIH Correspondence: Letter and Memo Preparation	12/6
Consolidated Purchasing Through Contracts	12/2
Buying From Small and Large Businesses on the Open Market	12/6
IMPACT System for Personnel Staff	11/19, 12/3, 12/19
<i>Personnel Management 496-6211</i>	
Basic Position Class. (enroll by 12/16)	2/7
Employee Relations for Personnelists	12/9
Qual. Analysis (enroll by 11/22)	1/8
<i>Special Courses 496-6211</i>	
Mid-Career Financial Planning	12/2
Break the Smoking Habit	1/14

The NIH Training Center, DCRT, and other training information is available on WYLBUR. Logon to WYLBUR and type ENTER TRAINING

### Lunchtime Concert Set, Nov. 25

A program of music by Schubert and Brahms will be presented on Monday, Nov. 25 from 11:45 a.m. to 12:45 p.m. in the 14th floor assembly hall, Bldg. 10.

Sponsored by FAES and the NIH Chamber Players, violinist Daniel Banner and pianist Carl Banner will perform Schubert's Duo in A Major, Opus 162, and Brahms' Sonata #3 in D Minor, Opus 108. All are invited to attend. □

### Disney Ice Show Tickets

Walt Disney's "World on Ice," featuring Roger Rabbit, Mickey and Minnie Mouse, Chip n' Dale, and other famous Disney characters, will be at the Washington Convention Center Dec. 10-15. R&W has tickets to three performances: Saturday, Dec. 14 at 12 noon (\$12.50 each) and at 3:30 p.m. (\$14.50 each); and Sunday, Dec. 15 at 3:30 p.m. (\$14.50 each). Tickets are available through any of the R&W stores. For more information, call 496-4600. □

## Children's Inn Gets New Executive Director

Robert N. Gray recently joined the Children's Inn at NIH as its executive director. He was formerly assistant executive vice president and staff director of the Greater Washington Board of Trade, where he served for 13 years. His 25 years in the Washington area has been a blend of service to the community and care for its people, particularly children. He has also worked with such organizations as For Love of Children, Sarah's Circle, the Cultural Alliance of Greater Washington, Junior Achievement of the National Capital Area, and the Corporation Against Drug Use.

"I could not be more enthusiastic about or committed to the work of the Children's Inn," Gray said. "It brings together all the strands of my personal and professional interests. The inn's focus on family is identical to my own. I intend to devote myself to its mission and look forward to a close and long association with its directors, staff, volunteers, and residents."

Regarding his plans for the inn, Gray says he wants, "an already smooth-running enterprise to be even more effective at assuring the best possible quality of life for kids who come to the inn. The inn is unique. It is a place where families can be with children during their medical treatment; it is a place where economic burdens can be reduced; and it is a place where kids and their families can interact with others experiencing similar stress. The holistic environment of the inn can reduce that stress and promote healing.

"Down the line we want to quantify the healing that is experienced here," he says. "I



Robert N. Gray

hope that we can model holistic care and communicate what we learn."

Another goal is to better understand, define, and strengthen the relationship between volunteers and residents. "We must be sensitive to the residents as we equip the volunteers to meet their special needs."

An additional challenge Gray sees is to strike a balance between what he recognizes as two inherently conflicting goals. "On the one hand, the Children's Inn must continue as a 'safe place' where families can come and be themselves—be just people." On the other hand, he says, the inn is, and should continue to be, a "showplace" in order to attract the resources to make it better and to be able to learn from it."

Gray concludes, "Our opportunity is to make life as good as it can be for as long as our residents are with us." □

### Radiation Safety Branch's Training Video Wins Award

*Radiation Safety Refresher Training*, the Radiation Safety Branch's 1990 video seen by more than 3,600 NIH'ers who work with radioactive materials in patient care or laboratories, won an honorable mention in the National Association of Government Communicators' annual "gold screen" competition.

The video's executive producer was Nancy Newman, a senior health physicist with the Radiation Safety Branch in the Division of Safety; the producer/director was Trish Evans of the Medical Arts and Photography Branch, NCRP.

Commenting on the video's attributes, the competition reviewers said it was "well-written, factual, informative and easy to follow."

The 12-minute video was produced to satisfy Nuclear Regulatory Commission regulations requiring yearly training to familiarize NIH personnel with recent regulatory changes, radiation safety problem areas, and NIH license and program changes.

In pre-video days, RSB conducted approximately 100 separate lectures using 12 different staff members to cover the material. Now all radionuclide users are notified of scheduled video showtimes held between July and November at several locations on campus.

If you would like to see the award-winning video, call 496-2255. □

### 'Nutcracker' Tickets Available

The R&W has tickets to upcoming performances of *The Nutcracker* by the Washington Ballet at Lisner Auditorium on the campus of George Washington University. Dates are Saturday, Dec. 21 at 7 p.m.; Saturday, Dec. 28 at 2 p.m.; and Sunday, Dec. 29 at 5 p.m. Tickets cost \$22 and are available at all R&W locations. □

*Man and Manometer***Van Slyke Exhibit Illuminates Soul of a Machine**

By Rich McManus

A couple of eminent "Van Slickers" visited NIH Oct. 18 to help open the newest exhibit in the DeWitt Stetten, Jr. Museum of Medical Research at NIH.

Drs. Rollin D. Hotchkiss and Reginald Archibald, professors emeritus at Rockefeller University, participated in a seminar designed to explain the workings and significance of an odd piece of equipment known as a Van Slyke manometric apparatus.

Located under glass in the conference room lounge area on the sixth floor of Bldg. 31C, the apparatus contributed mightily to both basic and clinical research between 1920 and 1960.

The apparatus, now supplanted by chromatography and spectroscopy, resembles some sort of glassblown hallucination from the set of a Frankenstein film. On top of that, it shimmies like a paint shaker at the press of a button.

Hotchkiss, a biochemist and geneticist best known for his DNA research, gave a history of



*Setting up a projector for the seminar on the Van Slyke apparatus are (from l) Archibald, Hotchkiss, and exhibit curator Dennis Rodrigues of the NIH Historical Office.* Photos: Ernie Branson

Archibald, a biochemist and pediatric endocrinologist, gave an overview of clinical applications to which the apparatus was put. A collaborator at Rockefeller with the instrument's inventor, Dr. Donald D. Van Slyke, Archibald noted that the Van Slyke machine helped scientists (known as Van Slickers) measure carbon dioxide concentration in blood, aided in diagnoses of diabetes and nephritis, and offered explicit quantitative measures of amino acids and other biological compounds. Van Slyke himself, reported Archibald, was tirelessly inventive and an eminent contributor to medicine, although he was not an M.D.

"Van Slyke didn't attend medical school, except as a teacher, but made great contributions to medicine nonetheless. He was a chemist who won the respect of clinicians," Archibald said.

The machine's inventor was editor of the *Journal of Biological Chemistry* from 1914 to 1924, and "his tenacious persistence wedded chemistry to medicine," Archibald noted. "(Van Slyke) unraveled mysteries of the blood, lung and kidney, revised the Army's chemical manual, masterminded the treatment of patients with oxygen, and improved our understanding of acid/base balance. He was also a remarkable teacher—many full professors and department heads were either trained by him or by people whom he had trained."

Hotchkiss reported that the NIH museum's call for a Van Slyke apparatus reached him in Albany.

"I last used the machine at Rockefeller University in 1948 or '49," he said, "and then I let it sit around for a few years. Finally I put

it up on top of a lab hood and promptly forgot about it while I went on with other work. When NIH called, I went back to Rockefeller and there it was. I cleaned it up a bit and here it is."

Among those who sat in on the seminar introducing the exhibit was NLM director Dr. Donald Lindberg, who had trained on the machine at Columbia during the waning days of its use.

Anyone wishing to see the exhibit, or who wants to know what the machine really did, may consult the Van Slyke manometer itself and an accompanying history brochure, written by exhibit curator Dennis Rodrigues.

"Whoever wrote that brochure really knows what this machine is all about," endorsed Archibald. "He can use my Van Slyke any time." □

**Open Season Scheduled For Thrift Savings Plan**

The Thrift Savings Plan (TSP) is having another open season from Nov. 15 through Jan. 31, 1992. FERS employees who were hired before July 1, 1991, as well as CSRS employees have an opportunity to change their current election, or make an initial election.

Eligible FERS and CSRS employees may elect to contribute to the G fund (government securities), C fund (stocks), and/or F fund (bonds). FERS employees may contribute up to 10 percent of their salary each pay period and will receive matching agency contributions on the first 5 percent. CSRS employees may contribute up to 5 percent of salary, but do not receive any matching contributions. FERS employees who do not contribute receive an automatic 1 percent agency contribution each pay period. They may choose to distribute this contribution among the three funds.

The features of the plan and directions on how to make a plan election or to change one's current withholding are described in the *Thrift Savings Plan Open Season Update* pamphlet, which will be distributed to eligible employees by their ICD personnel office. More detailed information is provided in the *Summary of the Thrift Savings Plan for Federal Employees* booklet and is available in each ICD personnel office. □

**Use/Lose Reminder**

Don't forget to schedule "use or lose" annual leave in writing no later than Saturday, Nov. 30. Questions concerning "use or lose" leave should be directed to one's ICD personnel office. □



*Flanking the Van Slyke manometric apparatus, the newest addition to the DeWitt Stetten, Jr. Museum of Medical Research, are Drs. Reginald Archibald (l) and Rollin D. Hotchkiss, who used the instrument.*

the instrument he bequeathed to NIH after using it in research from 1925 to 1949.

"We used it for the microanalysis of blood gases," he reported. "It helped define an early class of antibiotics and was used to study such substances as urea, amino acids, glucose and cholesterol.

"Old and young people have survived better because of the Van Slyke machine," he concluded.

Why call it a "machine" rather than an instrument, queried Dr. Victoria Harden, who directs the museum and heads the NIH Historical Office? "Machine was an endearment," chortled Hotchkiss. "It means it's part of your family."