Still The Second Best Thing About Payday

NIA/NIDA Poster Day Celebrates Decade of Student Learning
By Doug Dollemore

A few months ago, 18-year-old Bill Rogers knew little about aging. But after participating in the National Institute on Aging Summer Intramural Research Program, he has developed a clearer understanding of the aging process and its biological underpinnings.

"Working on projects involving osteoarthritis reminded me of how insidious many age-related diseases are," Rogers says.

Tiffani Bright, an information systems management major and Meyerhoff Scholar at the University of Maryland Baltimore County, explains her projects to NIA director Dr. Richard Hodes.

"Every step I take increases the size of miniscule tears that will eventually open into gaping weaknesses in my cartilage that could plague me 40 or 50 years from now. So just because there is no pain doesn't mean the steady process of aging isn't occurring."

Rogers, who will be a sophomore at Duke University this fall, is one of 42 students who participated in the NIA summer program and was among those who presented research findings at the 10th annual NIA and NIDA IRP Poster Day on Aug. 1 in the lobby of the Gerontology Research Center in Baltimore. Dr. Michael

Caused Mostly Unknown

Epidemiologist Hauser Traces Roots of Epilepsy
By Rich McManus

Occurring within the cloaked realm of the human cranium, epilepsy—a firestorm in the brain that can incapacitate a victim for seconds to hours—is a neurological disease whose cause, in about two-thirds of all cases, is unknown. Because it occurs in such an inviolate sanctum, epilepsy is most easily examined from without. Therefore medicine deploys its least invasive weapon—epidemiology—to probe the phenomenon from its margins, detailing whom it hits, and when, and in association with a great number of factors including age, prior medical history, habits (including drinking and drug use) and genetic legacy.

On hand in Lipsett Amphitheater June 18 to shed light on the issue was Dr. W. Allen Hauser of Columbia University's College of Physicians and Surgeons, whom host Dr. William Theodore, chief of the clinical epilepsy section, NINDS, called "clearly the leading world expert on the epidemiology of epilepsy."

"Most people find epidemiology sort of boring," Hauser began, because it deals in probabilities, large and ungraspable numbers,

NIH’s Last Glassblower Prepares to Exit
By Carla Garnett

Have you ever really needed a mouse milker? Where would you go if you wanted a contraption to sort rat waste? Ever seen a mosquito feeder (besides the occasional arm or leg during picnic season)? For more than four decades, NIH has never needed to look farther than Bldg. 13 for the man who not only knows each of these devices well, but also crafts them on demand. On July 23, Bill Dehn marked 40 years of wielding blowtorches at NIH. He will retire in January, and take with him NIH’s last vestige of the centuries-old tradition of glassblowing.
Gottesman, NIH deputy director for intramural research, was among the attendees.

Since its inception in 1993, more than 400 students from diverse ethnic and socioeconomic backgrounds have presented results of their summer research projects on NIA and NIDA IRP Poster Day. This year's class, ranging from high school to medical students, presented findings from a cornucopia of research areas including bioinformatics, cellular apoptosis and neurological disorders such as Parkinson's disease.

"One fundamental goal of this program is to stimulate, encourage and nurture a quest for knowledge in biomedical research among budding scientists," says Dr. Yolanda Mock, NIA biomedical recruitment coordinator. This year's participants say the program did that, and much more.

"My summer experience has far surpassed my goals," says Sundeep Viswanathan, a senior biochemistry honors student at the University of Texas, Austin. "Not only have I honed my scientific reasoning and learned valuable research techniques, but I have had the chance to speak with experts in many fields, which has opened my eyes to the endless possibilities available in research."

Students interested in participating in the 2003 NIA or NIDA Summer Intramural Research Programs can learn more at http://www.grc.nia.nih.gov/students/summeropps.htm. They also can email Mock, mocky@grc.nia.nih.gov, or Dr. Stephen J. Heishman, NIDA summer program coordinator, sheish@intra.nida.nih.gov.

Sundeep Viswanathan (r) discusses his poster, "Histone Deacetylase Inhibitors Induce Apoptosis in Diffuse Large B-Cell Lymphoma Cell Lines," with Dr. Dan L. Longo, NIA scientific director, and Dania Medina, a fellow student.
Dr. Samuel W. Cushman, chief of NIDDK's experimental diabetes, metabolism, and nutrition section, received the Banting Medal for Scientific Achievement at the recent American Diabetes Association meeting in San Francisco. The award is ADA's highest research honor, and it recognizes significant, long-term contributions to the understanding, treatment or prevention of diabetes.

Cushman was honored for basic science findings that were pivotal to explaining the relationship between insulin and glucose transporters. In the late 1970s, he and his then colleague L.J. Wardzala showed that insulin promotes the translocation of glucose transporters from intracellular space to the plasma membrane in insulin-sensitive cells. K. Suzuki and T. Kono at Vanderbilt University made the same finding independently.

When Cushman and Wardzala started their experiments, Cushman said researchers didn't know just how pervasive glucose transporters are. In an early experiment using fat cells, they asked whether an increase in insulin would raise either the number or the activity of glucose transporters in the plasma membrane that surrounds the cell. "We had no idea glucose transporters were anywhere else," Cushman says.

In 1978, the researchers claimed that insulin increased the number of transporters in the plasma membrane. They thought the transporters were somehow hidden and that insulin was needed to make them appear. "We wanted to know how 'cryptic transporters' could be seen. When we failed, we decided to see if they came from somewhere else."

Cushman and Wardzala next worked on intracellular membranes and found that they actually contained most of the glucose transporters. Finally, when they treated intact fat cells with insulin, they discovered that plasma membrane levels of glucose transporters increased. At the same time, the level of glucose transporters in the intracellular membranes decreased, which strongly suggested that intracellular glucose transporters moved outward in response to insulin.

Initially, most scientists thought this translocation hypothesis unlikely. But because Kono's lab at Vanderbilt was getting the same result using different techniques, "we thought we were on the right track," says Cushman. His and Wardzala's results were published in 1980 on a fast track in the Journal of Biological Chemistry. The reviewers' comments and criticisms were so extensive, says Cushman, "the review letter defined what we did for the next 10 years."

Another key finding by Cushman's lab showed that G proteins controlled glucose transporter functioning at the plasma membrane. During translocation of glucose transporters from the inside to the outside of cells, vesicles containing the transporters bind to and then fuse with the plasma membrane. Depending on the specific G protein and its activating agent, vesicle fusion either speeds up or slows down. When vesicle fusion speeds up, the number of glucose transporters increases at the plasma membrane, which in turn increases glucose uptake into cells. When fusion slows, glucose uptake declines.

According to ADA, "the discovery of intracellular glucose transporters, subsequently shown to be GLUT4, turned out to be not only a major breakthrough in understanding the molecular mechanism of action of insulin on glucose transport, but (also) of key importance to understanding the pathophysiology of insulin resistance and type 2 diabetes." GLUT4 is the dominant glucose transporter in white and brown fat and skeletal muscle. In people who are resistant to insulin, fat tissue loses some of its internal GLUT4 transporters, so there are fewer to go to the cell surface, says Cushman. In contrast, insulin resistance in skeletal muscle is caused by a defect in the translocation mechanism, which are responsible for the movement of the vesicles that carry the glucose transporters.

There's still a lot to be understood about trafficking, the two-way traveling of glucose transporters, says Cushman, who especially wants to understand the process in insulin-resistant people. He is now doing studies that rely on antibodies and fluorescent probes to track exactly where individual glucose transporters go in fat and muscle cells in normal and insulin-resistant animal models of human metabolic states, especially type 2 diabetes and obesity.—Anna Maria Gillis

**Have Premature Ovarian Failure (POF)?**

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attention deficit hyperactivity disorder (3-fold, but 4-fold if ADD only); mental retardation (9-fold); cerebral palsy (12-fold); a combination of retardation and CP (50-fold).

Hauser ended his talk by pointing out that pre- and perinatal health dangers (including seizures during infancy) are not risk factors for epilepsy, and noted that marijuana use appears, in his studies, to have a somewhat protective effect against epilepsy.

"We're hoping we can whittle down that 62 percent (of epilepsy cases) for which the cause is not known," Hauser concluded.

Orientation Fair Set, Sept. 18

The 3rd annual NIH Orientation Fair will be held Wednesday, Sept. 18 from 10 a.m. to 1 p.m. in Bldg. 10 on the B1 level in the exhibit area outside the Visitor Information Center. Based on the theme, "Ask me about the NIH," the event will showcase the wealth of professional and personal services that are available to trainees and employees.

"We hope the fair will give all participants a concise and complete grasp of campus resources, making them more capable more quickly and enriching their experience here," said Deborah Cohen of the Office of Education, which is sponsoring the event along with the Office of Research Services and the Work and Family Life Center.

Visitors will find more than 50 booths with representatives from the NIH Library, Office of Animal Care, credit union, parking and police, Work & Family Life Center, occupational safety and many others. They can sign up for email distribution lists, pick up giveaways and get answers to their questions. Sign language interpretation will be available. Individuals who require this or other accommodations should call 496-2427.

Lee Returns to Communications

Hugh Lee, who headed the information office at NIEHS from 1977 to 1994, when he retired, is back in the communications business, writing for the Environmental Protection Agency at its new $273 million facility just across a small landscaper's lake from NIEHS.

Almost 2 years ago, he returned to work under the EPA's Senior Environmental Employment Program funded by the National Caucus and Center on Black Aged, Inc. He spends 19.5 hours a week writing stories for an EPA newsletter. The employment program aims to keep senior environmental staff employed in the federal government, and provides money for salary and leave. Lee's career in communications began in the Washington, D.C., area, where in the late 1950s, he worked as a television news reporter.

A few years later he went to the Bureau of Public Roads, now the federal Department of Transportation, editing and narrating films. His next career move took him to the District of Columbia Commissioners' information office as a writer and photographer. From there, he joined NIH in the Division of Research Grants, where he wrote for the DRG newsletter. That position led him to NICHD, then to NHLBI, where he founded and directed the High Blood Pressure Information Center.

When NIEHS advertised to fill a position in the information office, Lee took the bait and applied, but his wife, Carol, was not thrilled at the prospect of moving to North Carolina. When they came down for the interview, they visited Emerald Isle on the state's Outer Banks. That apparently was all it took to change her mind. The Lees moved to Raleigh, where Hugh, Carol and one of their three children still live.

NIH Hosts Pavilion at Black Family Reunion

As part of its outreach efforts to address health disparities, NIH will participate in the 17th annual National Black Family Reunion Celebration Sept. 7-8 on the grounds of the Washington Monument. NIH has reserved a pavilion to conduct and support research that will result in improved health for all people. The National Council of Negro Women reunion attracts more than 500,000 people each year. All are welcome to attend. Admission is free. For more information about the NIH information booth, call Joan Lee of NEI (496-8990), Levon Parker of NINDS (496-3332) or Frederick Allen Wittington Jr. of OD (594-3591).
Although the delicate glass globe Dehn holds looks like it belongs in an art museum, it is actually more at home in the lab, sorting rat waste.

"Our main job is to create one-of-a-kind things that are not commercially available," Dehn explains. "When the scientists can’t buy what they need, we make it. When what’s available won’t do what they want, we modify it. And when something breaks, we repair it."

At its peak in the late 1970s and early 1980s, the Office of Research Services’ Biomedical Engineering and Instrumentation Branch had six glassblowers on staff, and most of them put in overtime producing the unique devices required for research. Labs and clinics on campus were using more than 50,000 glass units each year, many of them crafted to individual specifications and protocol requirements.

For decades, other labs came to NIH glassblowers for their unique research tools.

"These days many of the devices have been replaced by computer modeling," Dehn notes, "and a lot of the grants we used to work on are being sent to universities."

In addition, Dehn says, although glass is an ideal material for prototypes, less expensive and more flexible plastic is the material of choice for mass production of most clinical and laboratory devices.

"Now these are made of plastic, so they are more comfortable for the patient," he says.

James Sullivan, supervisor of ORS’s mechanical instrument design & fabrication section, which is operated on a fee-for-service basis, explains: "Due to the increased availability of commercial products and the popularity of plastic and disposable items, demand for in-house glasswork has declined. There is really no longer enough work to keep someone employed full time."

One by one over the last 10 years, each of Dehn’s colleagues has retired or moved on to other jobs. Last year, only Dehn and one other glassblower, Carroll Toms, remained. Due to fewer and fewer incoming requests, Toms had been assigned work in another instrumentation section before he retired a short time ago. With several patents to his credit and many more grateful scientists whose work he respected and aided, Dehn says he’s ready to live the retired life too.

"I’ll be really sorry to see him go," says Dr. Harry Saroff of NIDDK’s Laboratory of Genetics and Biochemistry. "He made some fine instruments for me. Many of them were fairly difficult to make because they had to be handled so gingerly. They were extremely delicate and fragile. It would have been a lot more expensive to have these items made outside. These were fairly complicated items that I needed for my experiments."

Saroff represents quite a few scientists who have visited Dehn over the years, requesting uniquely fabricated glasswork. Most times, the researchers came to Dehn with little more than an idea and a roughly scribbled sketch of the necessary item. From there, Dehn’s skill and creativity took over.

"I’ve always found him to be a highly qualified craftsman," Saroff recalls, describing one instrument—a jacketed reaction vessel—that Dehn crafted to help keep fluids at a constant temperature. "You seldom find that quality nowadays, but I’m old enough to remember the good old days."

Colleagues will miss not only Dehn’s technical skill with a glass tube and an open flame, but also his ability to make people laugh.

"Of course, there’s no replacement for Bill," Sullivan agrees. "He’s quite accomplished. More importantly, he has a historical knowledge of the research here that nobody else does. He can almost predict what a scientist will need."

"But we are also losing another ‘art’ of Bill’s—his sense of humor," Sullivan continues. "I think it would be recognized by most people who have worked with Bill or perhaps only encountered him for a brief period. He has maintained his humor through difficulties both personal and professional."

Even after Dehn leaves, ORS will continue to support scientists by helping to arrange contract glassblowing if necessary or by offering consultations on where to purchase necessary devices. "One way or another," Sullivan concludes, "we intend to provide the services we are currently providing."

Reflecting on the past 40 years on the job and describing one of his proudest moments, Dehn says...
he will mostly miss being involved in the research here. It was quite a few years ago, he remembers. He was producing lab devices for longtime NIDDK researcher Dr. Makio Murayama, who at the time was conducting studies on sickle cell anemia. Murayama—who was being acknowledged for the success of his research by an ambassador from Ghana—invited Dehn to a reception and introduced him to the African diplomat. The grateful ambassador heaped praises on the NIH'ers for the research and, subsequently, Murayama and Dehn were regaled with heartfelt tales of how research with the drug hydroxyurea was helping children in Ghana survive their disease and manage the pain of the disorder.

"Over the years I've worked for a lot of well-known researchers," recalls Dehn. "That day with Dr. Murayama and the Ghana ambassador was very special, though. I was very gratified to know that in some small way, I had something to do with it."

**HRDD Class Offerings**

The Human Resource Development Division supports the development of NIH human resources through consultation and provides training, career development programs and other services designed to enhance organizational performance. For more information call 496-6211 or visit [http://LearningSource.od.nih.gov](http://LearningSource.od.nih.gov).

- Processing Personnel Actions
  - 8/26-30
- Introduction to MS Excel 2000
  - 8/27
- Business Etiquette
  - 8/28
- IMPAC II Committee Management for SREA staff
  - 8/28
- Professional Service Orders
  - 8/28
- The Professional Office Manager II
  - 8/28, 29
- Introduction to Nutrition
  - 9/3-12/10
- Principles of Accounting I
  - 9/3-12/10
- Speaking on the Job-Part II: Presenting Yourself and Your Ideas
  - 9/3-5
- Travel for Administrative Officers
  - 9/3
- Advanced MS Word 2000
  - 9/4
- Foreign Travel
  - 9/4-5
- General Psychology
  - 9/4-12/18
- Intermediate MS Access 2000
  - 9/4
- Principles of Management
  - 9/4-12/18
- Human Relations in Management
  - 9/5-12/19
- Medical Terminology I
  - 9/5-12/5

**NIH Library Announces Fall 2002 Seminars**

Evidence-Based Medicine and Chemistry Resources are two new seminars offered this fall at the NIH Library. Free, hands-on seminars on 12 topics cover how NIH staff can effectively use the library's electronic resources. No registration is required. Seminars are held in the Library Training Rm., Bldg. 10. For more information, call 496-1080 or visit [http://nihlibrary.nih.gov/training.htm](http://nihlibrary.nih.gov/training.htm).

**Course on Beethoven's Quartets**

The FAES Graduate School at NIH is offering a Beethoven string quartet performance-lecture course this fall. All 16 quartets will be performed live, with lectures outlining each quartet. The class will be held Mondays from 5:30 to 7:30 p.m. The course is for all NIH music lovers, even those who can't read music. For information about registration (which must be completed by the end of August), call 496-7976 or visit [www.faes.org](http://www.faes.org).

**NIH Toastmasters Celebrate 20 Years**

The NIH Evening Speakers Toastmasters Club will celebrate its 20th anniversary on Tuesday, Sept. 10 from 7:30 to 9:30 p.m. at Positano Ristorante Italiano in Bethesda. All are invited to attend the event. Dinner costs $34.50. For details contact Cheryl McDonald, 435-2149, by Sept. 4. [http://nihrecord.nih.gov](http://nihrecord.nih.gov)
NIAMS Celebrates a Milestone in Health Disparities Research

July 18 marked the first anniversary for the NIAMS Community Health Center, NIH's first community-based clinic devoted specifically to health disparities research in rheumatic diseases.

To celebrate, the National Institute of Arthritis and Musculoskeletal and Skin Diseases held a reception that included community leaders from the greater Washington area; medical experts from area hospitals and academic institutions; NIH staff; NIAMS advisory council members; and staff and patients of Unity Health Care, Inc.

Through a partnership with Unity, which includes a $1-per-year rental of a medical suite in one of their health centers, NIAMS connects with the local African American and Hispanic/Latino communities, two groups disproportionately affected by some rheumatic diseases.

The health center serves as a training facility for researchers, physicians and students interested in rheumatology and minority health. It also provides the local community with access to specialty care, clinical studies and health information, as well as employment and training opportunities. The center is located at 3020 14th Street, N.W., Washington, DC 20009. For more information, call (202) 673-0000.

Participants at the celebration include (from l) Dr. Janelle Goetchens, Unity GMO; Vincent Keane, Unity CEO; Dr. Elias Zerhouni, NIH director; Dr. Ruth Kirschstein, NIH deputy director; Dr. Peter Lipsky, NIAMS scientific director; Dr. Stephen Katz, NIAMS director; and Dr. Gregory Dennis, NIAMS fellowship program director.

NIAMS advisory council member Dr. Matthew Liang (l) enjoys a moment with Zerhouni (c) and Katz.

NIAMS community partner Dr. Warren Ashe of Howard University (l) greets Lipsky (c) and Zerhouni.

Tae Kwon Do Beginner’s Class

The NIH Tae Kwon Do School is offering a beginner’s class for adults and mature teens starting Sept. 9. The class will meet in the Malone Center (Bldg. 31C, B4 level, next to the NIH Fitness Center) from 6 to 8 p.m. on Mondays and Wednesdays, and will continue for approximately 2 months until participants can be integrated into the regular school training. Dues are $40 per quarter; a uniform costs $30. Interested persons are welcome to watch regular training sessions. For information, call Andrew Schwartz, 402-5197, or visit the web site at http://www.recgov.org/r&w/nihtaekwondo.html.
Epilepsy is not uncommon following a stroke, and the risk endures even decades after the stroke has occurred.

Dr. Alan P. Koretsky, chief of NINDS’s Laboratory of Functional and Molecular Imaging, recently received the Gold Medal award from the International Society of Magnetic Resonance in Medicine for his significant contributions to research in this field. Koretsky, who also serves as director of the NIH MRI Research Facility/Mouse Imaging Facility, was particularly recognized for his and his colleagues’ pioneering work on transgenic mice, the use of Mn2+ as a paramagnetic tracer for brain studies, and perfusion measurements using arterial spin labeling.

Koretsky has long been interested in bioenergetics and development of non-invasive imaging techniques to study physiological processes. His laboratory developed novel techniques to measure a variety of functions in the brain such as regional blood flow and neuronal tract tracing by MRI.

and such statistical arcana as confidence intervals. “Even the Epilepsy Foundation has no idea where its numbers (on the incidence of epilepsy in the population) come from... The fact is, two-thirds of the time or more, we can’t answer why convulsive disorders occur,” he said.

In an attempt to establish the cause of epilepsy, science has looked for a triggering event, such as a febrile seizure (a convulsion associated with fever), then examined whether the disease developed down the line. But you can do chicken-and-egg thinking, too: Did some unknown factor lead to the febrile seizure, and then subsequent epilepsy? Various causal directions are hypothesized, and Hauser focused on pathways of association taking the form of some exposing event—say stroke, or head injury, or central nervous system infection—which is then followed by epilepsy. His research has shown that those three precursors each result in a 20-fold increase in risk of the disease. Other risk-elevators for epilepsy include Alzheimer’s or any other progressive neurological disease, and brain tumor. And a classic Vietnam War-era study showed that a bullet through the head inflates epilepsy risk 600-fold.

Employing data from Iceland, where whole-population information is accessible, Hauser said unprovoked seizures occur in approximately 5½ of every 100,000 people. The ratio is 57/100K in males and 33/100K in females. Worldwide, the ratio appears to be about 43 cases in every 100,000, with males having a slightly higher risk globally. “That leads us to wonder, is there something about being female that’s protective?” Hauser asked.

Age is also a risk factor for epilepsy. “The risk is high in the first year of life,” Hauser said, “and falls dramatically at midlife, then increases dramatically to its highest incidence in the oldest age group.” A study in Harlem showed that age alone is associated with a 30 percent elevation in risk of epilepsy for every decade past age 20, he reported.

Around 6 percent of epilepsy cases can be tied to alcohol abuse (heavy drinking is the equivalent of severe head injury, Hauser noted), and nearly 9 percent of cases follow head trauma. Epilepsy is not uncommon following a stroke, and the risk endures even decades after the stroke has occurred. In those who suffer a seizure after a first stroke, 20 percent develop epilepsy within 5 years, “and the risk goes up after that. Even 20 years later, the risk is elevated 3-fold... The risk is substantial—it’s greater than many people think,” Hauser said.

“And it’s long-term.” While stroke results in elevated epilepsy risk, a TIA (transient ischemic attack), interestingly enough, results in no increased susceptibility, provided there is no permanent damage, he said.

A person who suffers a seizure in the first week after a stroke has a 30 percent higher risk of developing epilepsy later on, he said. “The first seizure may beget later seizures, but it is more likely that this event is a marker for severity or location of stroke.”

A ruptured cerebral aneurysm also elevates epilepsy risk; within 5 years of such an event, almost 30 percent of survivors develop the disease.

Central nervous system infections cause epilepsy, he continued. “They set up the milieu for it,” observed Hauser, showing evidence that encephalitis results in a 15-fold increase in risk.

The litany he recited had a common theme: if something bad happens to the brain, epilepsy often results eventually. This was true for cases of brain injury: “There is a 15 percent increase in risk in the first few years following mild injury,” Hauser stated. “For moderate trauma (resulting in unconsciousness for a half-hour to 24 hours), the risk is 3-fold, and for severe trauma, the risk is 20-fold.” Even 10 years after a head injury of any severity, the epilepsy risk is elevated, he said. “Whatever it is that’s happening is not short-term.” (Playing tackle football is not associated with any increase in epilepsy, he observed, nor does boxing lead to the disease.)

Alzheimer’s disease, too, elevates risk: “There is a 6- to 10-fold increased risk, compared to age-matched normal controls,” Hauser said. “[AD is] a potent predictor of the disease.”

Other ailments associated with epilepsy include depression, hypertension and migraine. Those who suffer major depression have a 6-fold increase in epilepsy risk. In a study population of those over age 50 with hypertension associated with left ventricular hypertrophy, there was a 9-fold increase in epilepsy risk, though a therapy of diuretics appears to reverse that risk, and may be an important adjunctive therapy, Hauser said. And in a study of adults and children, migraine headache appears associated with a 4-fold risk, and if it occurs with an aura in children, risk goes up to 10-fold (adults with aura have a 3-fold risk).

Of the two kinds of epilepsy—partial and generalized—a specific gene has been found only for the latter type, Hauser reported.

Alcohol, he said, is clearly a risk factor. “Abstainers have a slightly increased risk. Those who consume two drinks a day seem to be okay with respect to risk. But at 3-4 drinks a day and up, the risk increases.”

Other elevators of risk include: a history of