

# nih record



ABOVE • When's spring, again? Campus frog ponders the same question we're all asking. See more photos, p. 7.

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### Train Mind to Change Brain?

## Visualizing Future May Help Weight Loss, Epstein Says

By Belle Waring

**D**r. Leonard H. Epstein of the University at Buffalo has found that visualizing a positive future event can help control the impulse to overeat.

"This is two ideas put together: the motivation to eat and the inability to delay gratification," he said. "This is a central idea to people doing research on drugs, now applied to studying obesity."

The SUNY distinguished professor of pediatrics and chief of behavioral medicine recently discussed his research results in Natcher Bldg. An expert in childhood obesity, Epstein is known for a warm and open teaching style. His talk, "Reinforcement Pathology: Lead-foot and Worn Brakes," was sponsored by the Office of Behavioral and Social Sciences Research.

SEE EPSTEIN, PAGE 6



Everybody wants immediate gratification, but some people have a harder time than others in resisting their impulses, says Dr. Leonard H. Epstein. He is finding ways to counter that tendency.

### Trash Talk

## Cuervo Explains How Our Cells Discard, Recycle Matter

By Dana Steinberg

As we learn more about the inner workings of cells, we're uncovering clues that may help us delay the effects of aging and disease. It all begins with lysosomes—the cannibals of the cellular world.

Within each cell, a lysosome is a sac of enzymes that digests anything in it. The lysosome devours proteins, lipids, even pathogens that enter from outside the cell, as well as components within the cell. The nutrients get broken down and recycled while the



Dr. Ana Maria Cuervo

SEE CUERVO, PAGE 8

## Brawley Calls for 'Rational, Evidence-Based' Medicine

By Eric Bock

Inefficient, unequal and irrational. That's how Dr. Otis W. Brawley described the United States' health care system at a recent Contemporary Clinical Medicine Great Teachers Grand Rounds lecture.

"We spend a lot of time focusing on treating illness as opposed to preventing people from getting illness," said Brawley, chief medical and scientific officer of the American Cancer Society and a former NCI scientist.



Dr. Otis W. Brawley

SEE BRAWLEY, PAGE 4





## briefs

### Neuhauser To Present at DDM Seminar

The Deputy Director for Management (DDM) announces the second DDM seminar of the 2013-2014 series "Management and Science: Partnering for Excellence." The event on Thursday, Apr. 17 from 11 a.m. to 12:30 p.m. in Masur Auditorium, Bldg. 10, will feature Peg Neuhauser, who will discuss "Breaking Down Silos in Your Organization." She will focus on building connections and strategies and the power of informal relationships.

Videocasting and sign language will be provided. Individuals who need reasonable accommodation to attend should call (301) 496-6211 or the Federal Relay Service at 1-800-877-8339.

For details about the series, visit [www.ddm-series.od.nih.gov](http://www.ddm-series.od.nih.gov) or call (301) 496-3271.

### STEP Forum on Successful Aging, Apr. 29

The staff training in extramural programs (STEP) committee will present "Live Long and Prosper: Successful Aging in Our Time," on Tuesday, Apr. 29 from 9 to 11 a.m. in Rockledge II, Rm. 9100. An information fair will be held from 11 a.m. to noon in Rm. 9112.

Aging is inevitable. What are the biological mechanisms governing aging? How do psychological, environmental and social factors affect successful aging? Translational research shows that we can influence how we grow old and improve the quality of our senior years. Join us as we explore the science and practical aspects of living longer and prospering.



*Last year's Earth Day event garnered gardening enthusiasts of all ages.*

### Earth Day 2014 Is on Its Way to an NIH Site Near You, Apr. 24

It is that time of year again. Flowers blooming, birds chirping and NIH's annual Earth Day event. This year, the "Plant a Seed, Grow a Healthy Future" themed celebration will be held on Thursday, Apr. 24 from 10 a.m. to 2 p.m. in front

of Bldg. 1, in conjunction with Take Your Child to Work Day.

Come visit demos, exhibits and displays by the NBC Channel 4 Storm Team weather truck and meteorologist Veronica Johnson, National Geographic, R&W seedlings giveaway, Montgomery and Prince George's County recycling programs, Baltimore Aquarium, Smithsonian Institution, Nature Conservancy, Scales and Tales and the NIH Bicycle Commuter Club. Attendees can take a spin on the NIH bike to generate energy or take a nature walk around the NIH stream from 10:30 a.m. to 12:30 p.m.

Local food trucks, including Ben & Jerry's and Chick-fil-A will also be on campus to provide discounted food options for attendees. This is an NIH zero-waste event: all waste will be either composted or recycled. NIH employees at local offsite locations may wish to take advantage of the extra shuttles provided for transportation to and from the Bethesda campus that day.

In addition, NIH's Bayview campus in Baltimore will host a flower-planting event, seedling handout, "Spin the Wheel" question & prize game and a recycling collection for toner cartridges, eyeglasses, light bulbs and personal batteries.

NIHES in Research Triangle Park, N.C., is hosting a joint effort with the EPA to have speakers educate attendees on invasive species. There will be a campus walking tour to highlight and identify such species. NIHES will also host a cleanup of the campus lake and will launch an "Adopt-a-Highway" event during Earth Week.

NIH on Executive Blvd. will host a music/film swap on Earth Day, with collections running from now to Apr. 18. Materials can be dropped off at any of four NIH locations: Bldg. 10, 2nd Fl. cafeteria; NSC 6th Fl. Rm. 6140; NSC 7th Fl. Rm. 7170D; and NSC 7th Fl. Rm. 7217.

NCI Shady Grove will hold its Earth Day event from 11 a.m. to 1 p.m. with a recycling exhibit, book swap, compost demonstration and lots of other table exhibits.

Consider volunteering your green ideas, time and talents to the Earth Day planning committee. If interested, contact Danita Broadnax at [broadnax@mail.nih.gov](mailto:broadnax@mail.nih.gov). Check out the full list of special Earth Day activities and events for all NIH facilities at <http://nems.nih.gov>.

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NIH Record Office Bldg. 31, Rm. 5B41  
Phone (301) 496-2125 Fax (301) 402-1485

Web address <http://nihrecord.od.nih.gov>

#### Editor

Richard McManus  
[Rich.McManus@nih.gov](mailto:Rich.McManus@nih.gov)

#### Associate Editor

Carla Garnett  
[Carla.Garnett@nih.gov](mailto:Carla.Garnett@nih.gov)

#### Staff Writers

Dana Steinberg  
[Dana.Steinberg@nih.gov](mailto:Dana.Steinberg@nih.gov)

Belle Waring  
[Belle.Waring@nih.gov](mailto:Belle.Waring@nih.gov)

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*NIH...Turning Discovery Into Health*

# nih record



Dr. Bill Gurley of the University of Arkansas

## NCCAM Lecturer Explains Herb-Drug Interactions

By Ellen O'Donnell

Herbal and other dietary supplements are easily found on store shelves, near the aspirin and antacids. But does that mean they are safe? Dr. Bill Gurley delved into a key aspect of this seemingly simple, but actually complex question when he spoke on herb-drug interactions as part of NCCAM's Integrative Medicine Research Lecture Series. He explored the negative effects that can occur if supplements—such as energy “shots” and drinks, weight-loss aids and herbal medicines—interact with conventional drugs, potentially affecting drugs' concentrations in the body and their clinical effects.

A professor of pharmaceutical sciences at the University of Arkansas for Medical Sciences College of Pharmacy and director of the UAMS clinical pharmacokinetics research laboratory, Gurley offered numerous insights to the NIH audience.

He set the stage with recent survey findings, including that 20 to 30 percent of people taking prescription drugs also take herbal supplements, yet less than 40 percent of patients using herbal supplements tell their health care providers of the use. Thus, the potential for herb-drug interactions may be present for consumers while their providers are unaware of it. “Because elderly people are our greatest consumers of conventional medications, they may be at increased risk,” Gurley said.

The mechanisms of herb-drug interactions are either pharmacodynamic (the herb has pharmacological properties either similar to or opposite those of the drug) or pharmacokinetic (the herb affects drug metabolism, usually by inducing or inhibiting the action of key enzymes and/or transporters). In this field of research, Gurley said, laboratory findings implying an interaction do not always translate into a problem in people. The best way to find out, he said, is prospective clinical studies.

Herb interactions can occur not only with medications, but also within herbal products. Many supplements contain multiple herbs; when that abundance of biologically active plant compounds combines, the result can be strong synergistic effects. Gurley described cases in which taking supplements containing stimulants such as caffeine, guarana, yerba maté, green tea or bitter orange—in excess, in combination, too quickly or with vigorous exercise (especially under hot conditions)—has led to emergency room visits and even fatalities (see sidebar).

He emphasized, “Most herbal supplements do not present a serious drug-interaction risk.” Gurley added, however, that most supplements' effects typically are also minimal, either from poor dosage form performance (inadequate disintegration or dissolution) or from being extensively metabolized before reaching the systemic circulation. But he cautioned that manufacturers are developing new technologies, such as liposomes, to address such issues. While these new technologies could help make an herb more available in the body, they could also increase risks for toxicity and/or interactions. Furthermore, they have been little studied in randomized, controlled trials, he said.

Gurley's lecture is available at <http://videocast.nih.gov/summary.asp?Live=13727&bhcp=1> and will be added to NCCAM's Online Continuing Education Series ([nccam.nih.gov/training/videlectures](http://nccam.nih.gov/training/videlectures)) later this year. 📺

### A Major Culprit in Interactions

Far and away the most problematic herb for herb-drug interactions is St. John's wort, said Dr. Bill Gurley. It has a very high drug-interaction risk, rendering most drugs ineffective in the body, including birth control pills, anti-coagulants, antidepressants, antiretrovirals, antiseizure drugs and immunosuppressants. He provided an example of how serious those interactions can be.

In 1999, Gurley received a call from one of his institution's transplant surgeons concerning a young patient who had had a kidney transplant 5 years earlier. Her cyclosporine levels kept falling, despite increased doses, and no one could figure out why. “The way they found out,” Gurley explained, “was when she mentioned to the dietitian on the transplant team that she was taking St. John's wort because she felt depressed. Long story short, [I confirmed that there was an interaction], she was taken off St. John's wort and about a week later her cyclosporine levels just skyrocketed. We finally got them back under control. Unfortunately, in her case, acute rejection evolved into chronic rejection, she lost her graft and she had to go back on dialysis and back on the transplant list. And this is just one of four such cases at our center.”

Since the late 1990s, Gurley added, articles from around the world have reported that using St. John's wort affects cyclosporine concentrations and has led to rejection of heart, liver and kidney transplants.

### Inn Hosts Tour, Luncheon

*The Children's Inn at NIH hosted a tour and luncheon on Mar. 18 for the spouses and partners of the institute and center directors. The group learned about the inn's programs and services and made Thoughtful Treasures for the children's mail boxes. On hand were (front row, from l) Barbara Mason, Sandy Nakamura, Susan Gardner, Diane Baker and Kevin Norris. At rear are (from l) Pam Sieving, Kirstie Saltsman, Dr. Sherry Mills, Norman Schiff, Elaine Gallin, Brigid Guttmacher and CIT Director Andrea Norris.*





## BRAWLEY

CONTINUED FROM PAGE 1

### Left:

*Brawley greets Dr. Fred Ognibene, Clinical Center deputy director for educational affairs and strategic partnerships, at the lecture.*

### Right:

*"In our health care system, some people overconsume resources, meaning they get unnecessary care," said Brawley. "Some people under-consume, meaning they don't get the care they need."*

PHOTOS: ERNIE BRANSON

According to Brawley, in 2010, U.S. health care expenditures reached \$2.6 trillion, roughly \$8,000 for each American. That's more than any other country in the world. Yet the U.S. lags behind many developed countries in such key health indicators as life expectancy and infant mortality.

"In our health care system, some people over-consume resources, meaning they get unnecessary care," he said. "Some people under-consume resources, meaning they don't get the care they need."

Brawley added that cancer mortality rates reflect this health inequity. Overall, the cancer mortality rate has declined by about 20 percent in the past 20 years. He attributes the decline to a decrease in smoking, improved treatments, early detection and cancer awareness. However, not every population is benefitting from these advances.

In many cases, stark differences in the availability of treatment exist between underserved minorities and other Americans. For example, African-American women diagnosed with breast cancer are more likely to die from the disease than white women with a similar diagnosis. In 2010, the disparity between the two populations was greater than in any other year previously. Similarly, African Americans diagnosed with colorectal cancer are also more likely to die from the disease than are whites with the same diagnosis.

Brawley also charged that practitioners have a

history of ignoring evidence-based medicine, particularly when it comes to the limitations of cancer screening. In 2011, the National Lung Screening Trial found that lung cancer screening can reduce the risk of death by about 20 percent for adults who are at least 55 years old and have smoked a pack of cigarettes a day for 30 years or adults who have quit smoking in the past 15 years. However, 80 percent of lung cancer diagnoses still resulted in death.

The trial also found that almost a quarter of adults screened will need further testing, such as a chest x-ray, lung biopsy or surgery. Roughly 24 out of 25 adults who receive further testing will not have lung cancer. Complications from further testing may lead to permanent disability or even death.

Today, researchers are using genomics to identify the genetic causes of different types of cancer. They hope to use what they learn to provide the foundation of individualized therapeutic approaches for different types of cancers.

"That 5-millimeter lesion may be genetically programmed to stay there and never grow," Brawley said. "Or it may be genetically programmed to grow, spread and kill. This may allow us to treat those that need to be treated and spare those that do not need treatment." <sup>1</sup>

## Groft, NIH Rare Diseases Advocate, Retires

Throughout his career, NIH rare diseases research advocate Dr. Stephen Groft has dedicated himself to advancing research on the thousands of rare diseases and conditions that affect millions of people. A public servant for more than four decades, he is known to many as a visionary champion of rare diseases research.

Groft recently retired from his position as director of the Office of Rare Diseases Research in the National Center for Advancing Translational Sciences. He leaves a 30-year legacy of advancing rare diseases research and improving the lives of thousands of patients. Dr. Pamela McInnes, NCATS deputy director, will serve as acting director of the office during the search for a new ORDR director.

“The enormous growth in rare diseases research at NIH is a legacy of Steve’s leadership,” said NCATS director Dr. Christopher Austin. “Rare diseases are no longer a curiosity on the periphery of the biomedical research enterprise. They now are central to the research agenda and that is due in large part to Steve’s vision, dedication and effectiveness.”

Groft’s journey began in a personal way. “Growing up in the 1950s, I had friends and neighbors who were stricken with diseases that had few or no effective treatments,” he said. Seeing how these devastating diseases affected his small-town community remained with him throughout his career.

These personal connections led him to the Food and Drug Administration and NIH, where he worked to prioritize rare diseases research and drug development. He also served in a variety of advisory roles to national leaders, including congressional and White House representatives, to influence the national agenda on rare diseases research.

In 1986, Groft was appointed executive director of the National Commission on Orphan Diseases. The group was charged with identifying gaps in rare diseases research, patient care, regulatory issues, insurance coverage and related areas. In 1989, he joined NIH as rare diseases coordinator and special assistant to the associate director for science policy and legislation. He went on to serve in many roles at NIH, including director of ORDR.

Groft was instrumental in establishing the Rare Diseases Clinical Research Network, launching the NIH Undiagnosed Diseases Program, contributing protocols to ClinicalTrials.gov, creat-



*Dr. Stephen Groft*

ing the Global Rare Diseases Patient Registry and Data Repository and forming the Genetic and Rare Diseases Information Center. In all of these efforts, he was an effective collaborator, bringing together NIH institutes and centers, patient advocacy groups, regulatory agencies and biopharmaceutical companies to advance the understanding and treatment of rare diseases. In addition, he worked to implement the recommendations of the National Commission on Orphan Diseases as well as legislative mandates, including the Rare Diseases Act of 2002.

He has received more than 25 honors and awards, including the Global Genes | RARE Project Henri J. Termeer Award for Lifetime Achievement in 2013, the National Organization for Rare Disorders Medal of Honor for “Vision and Pioneering Guidance” in 2013, and the Social Security

Administration Commissioner’s Appreciation Award for assistance to the Compassionate Allowance Initiative in 2012.

“I often heard Steve say, ‘We’ve got to bring people together and do something,’” said Austin. “Steve accomplished an enormous amount during his long career and it is up to us now to continue his legacy of action and bring his dream of treatments for all patients with rare diseases to reality.”

### Postbac Poster Day Set, May 1

Postbac Poster Day is scheduled for Thursday, May 1 at Natcher Conference Center from 10 a.m. to 3:30 p.m. Dr. Sharon F. Terry, president and chief executive officer, Genetic Alliance, will deliver the keynote address at noon. The keynote will be followed by presentation of mentoring award(s) to NIH investigators selected by the postbacs. Poster session I will take place from 10 a.m. to noon; poster session II lasts from 1:30 to 3:30 p.m.

At Poster Day, postbacs share research they have been conducting at NIH and at the same time develop their scientific communication and networking skills. Posters will be reviewed by teams composed of graduate students, postdocs and staff scientists. Authors of the top 20 percent will receive a letter acknowledging their accomplishments.

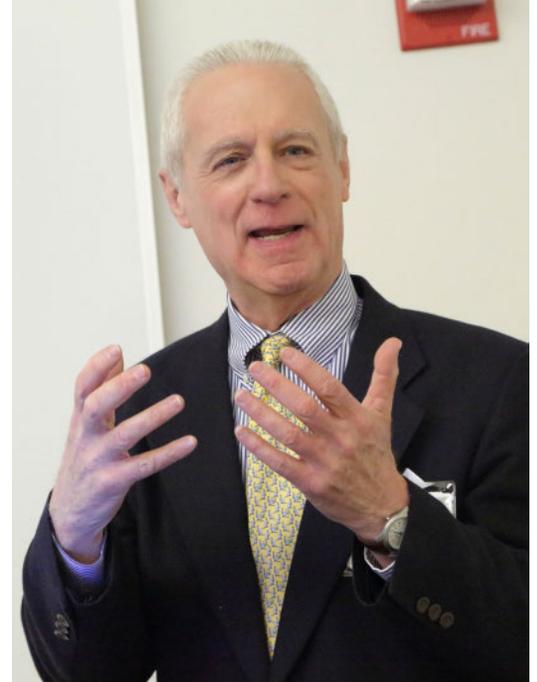
Investigators, staff scientists and scientific administrators can make an important contribution to the event by visiting posters and engaging authors in discussion. For more information, visit [https://www.training.nih.gov/postbac\\_poster\\_day](https://www.training.nih.gov/postbac_poster_day).

## EPSTEIN

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“I want to talk about how people make choices,” he said, “both for now and for the future; and how to delay immediate gratification for the long term.”

We eat for two reasons: to keep our bodies stable and for pleasure. The “reinforcing value” of food describes how hard someone will work to get access to it.



*Epstein proved to be an engaging speaker at NIH.*

PHOTOS: ERNIE BRANSON

***“Food is a powerful reinforcer. In animal models, it’s even more powerful than heroin and cocaine... and it’s strongest in food with a high sugar content.”***

“Food is a powerful reinforcer,” Epstein said. “In animal models, it’s even more powerful than heroin and cocaine...and it’s strongest in food with a high sugar content.”

“Babies respond right away to a sweet reward,” he continued. “It’s built into the limbic system”—a collection of deep brain structures common to all mammals.

The human infant’s brain already has a dopamine reward system that confirms milk is sweet and delicious. Dopamine is a versatile brain chemical that plays many roles, including how we register and reinforce pleasure.

So infants know how to eat, but learning to delay gratification comes much later. The prefrontal cortex (the front of the brain) is vital for “executive function” including long-term planning, judgment and self-control. And it’s not fully developed until the mid-twenties, so “a 12-year-old may not have the cognitive apparatus necessary to resist.”

Epstein illustrated this concept with a video clip of the famed Stanford “marshmallow experiment” in which young children were offered a choice: a single treat immediately or multiple treats if they were able to wait.

The sight of children with a tempting snack was endearing and funny, yet the implications were bracing. Follow-up studies found that, in general, children unable to wait grew up to be “more obese, had more contact with the criminal justice system and less education...”

Everybody wants immediate gratification, but some people have a harder time than others

in resisting their impulses. Epstein has seen a connection between impulsivity and differences in the prefrontal cortex, visible on brain-imaging studies.

In an automotive metaphor, he called this “lead-foot and worn brakes.”

“Obese people become sensitized [to high-calorie foods],” he explained, “so the more you eat, the more reinforcing it becomes.”

If you eat sweets over and over, the brain’s reward system creates the craving for more—what Epstein calls “reinforcement pathology.” This pathology, he said, is the interaction of the reinforcing value of food (lead foot) with the inability to delay gratification (worn brakes).

As a result, overweight and obese people have a harder time shifting their attention from current to long-term rewards. Epstein calls this “delay discounting”—our human tendency to discount, or undervalue, the merits of waiting.

Anyone, especially children, can act in haste, without thinking decisions through. Too much delay discounting is associated with overeating, over-shopping, drinking too much, abusing drugs and gambling.

Here’s the good news: “Now we can teach people how to reduce delay discounting, where they learn how to mentally simulate the future in order to moderate present behavior...We do this all the time. Before I came here, I said to myself as I was putting the slides together, which are people going to like?”

Epstein has refined and quantified this as episodic future thinking (EFT).

EFT teaches people to think about a long-term

goal or event they are looking forward to by encouraging them to visualize a future event.

“The effect depends on how vividly they imagine and how positive the event is,” said Epstein. Interestingly, “none [of the visualizations our subjects chose] were food-related.”

Subjects also used “tags,” or cues to initiate the EFT, such as moving their watch to the opposite wrist—to remind them to focus.

Athletes who are using visualization techniques to improve their performance, he said, “basically do a variation of EFT...Whatever the possibility is, they play it over and over in their minds, exactly the thing we’re talking about, only we’re putting it into practice for health behavior change.”

During the discussion, Epstein agreed on the importance of exercise in memory training: “Think how much executive function a [basketball] point guard has to have. Sports require a lot of self-regulation, planning, cognitive flexibility and working memory.”

In his earlier work, Epstein showed how overweight and obese women can become equally capable of the impulse control that lean women exhibit.

His current research involving mentally simulating future events is positive news for people who have struggled to lose weight.

“It shows that when people are taught to imagine, or simulate the future, they can improve their ability to delay gratification.”

And he’s optimistic about the future: “We’re doing our first field study...People are going into the college cafeteria, and right before they purchase, they listen to their tags. It’s really had a big effect on people’s ability to regulate their eating. We plan to follow this up with a clinical trial using EFT as a component of family-based treatment for pediatric obesity.”

A videotape of Epstein’s talk is available at <http://videocast.nih.gov/summary.asp?Live=13881&bhcp=1>. 📺



### Winter 2014 Was for Snow Lovers

Call them “snowfodils.” These discouraged stalks were shrouded in snow that fell the week of Mar. 24. In many years, the daffodils have come and gone by that date. But the chill of winter 2014 kept them abed until late March, and even then it was too early for comfortable display.

At right, this chilly frog was sighted just outside Bldg. 37, near the new Porter Bldg. You can almost hear Kermit wearily asking, “When will this stuff go away?”



Below, the winter of 2014 was like one of those horror movies where the villain, once thought dead, keeps coming back to life. It cannot be said with confidence, even in April, that we won’t see another flake. The most enduring evidence of winter is the “NIH glacier.” Examples can be found on the shady sides of campus parking structures, where plowed snow has been dumped. The photo below shows the west side of MLP-9. Anyone care to wager when the last evidence of snow disappears?

PHOTOS: BILL BRANSON, RICH MCMANUS



## CUERVO

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unusable waste gets destroyed. This process—the breakdown, recycling and disposing of cellular components—is known as autophagy.

Autophagy helps maintain cellular energy balance, contributes to immune health and serves a quality control function inside the cells by eliminating damaged or abnormal components. As we age, the activity of these pathways tends to decrease. Consequently, certain neurodegenerative diseases associated with aging may in fact be due to problems with these pathways.

*“If you have cells in which autophagy is not working properly, they’re going to be energetically compromised, they may not respond so well to nutritional stresses. They’re also going to be more vulnerable to the attack of pathogens.”*

Dr. Ana Maria Cuervo, a world-renowned expert on autophagy, and her lab team are studying these lysosomal pathways, particularly how to maintain their functionality and repair them. Professor and co-director of the Institute of Aging Research at Albert Einstein College of Medicine, she delivered the annual NIH Director’s Margaret Pittman Lecture on Mar. 19, titled, “Did You Remember to Take Out the Trash? Your Cells Sure Did!”

“If you have cells in which autophagy is not working properly, they’re going to be energetically compromised, they may not respond so well to nutritional stresses. They’re also going to be more vulnerable to the attack of pathogens,” said Cuervo. “They will have problems with their ability to remove all this garbage, all the abnormal components...[This in turn leads to] progressive loss of cell function, which is characteristic of aging and disease and in many cases can lead to cell death.”

Cuervo’s lab is working with neuroscientists to study the proteins that accumulate in patients with neurodegenerative diseases such as Alzheimer’s, Parkinson’s and Huntington’s. She said that disease often starts when these proteins become damaged and cannot penetrate the lysosome’s membrane.

“To make it all worse, you’re getting old and aging is interfering with the activity of these pathways,” she said. “If we can slow down the aging of these lysosomal pathways, we might be able to maintain or sustain ability or activity



*Cuervo, co-director of the Institute of Aging Research at Albert Einstein College of Medicine, delivers the annual Pittman Lecture.*

PHOTOS: ERNIE BRANSON

enough to eliminate part of these pathogenic proteins and slow down the disease.”

Autophagy can prevent cells from starving, as proteins and other nutrients entering the lysosome are split and can be used to produce energy. Cuervo said preserving autophagic activity helps lower intracellular accumulation of damaged proteins while improving organ function.

Advances in the study of impaired autophagy may help us slow down the aging process and delay the onset, or reduce the severity, of certain diseases. This area of research may also hold the key to developing novel therapies to treat a wide range of age-related disorders.

The lecture was held in tribute to the late Dr. Margaret Pittman, NIH’s first female lab chief. She joined the NIH staff in 1936 and made significant contributions to microbiology and vaccine development. Pittman was chief of the Laboratory of Bacterial Products, Division of Biologics Standards, from 1957 to 1971. ●

## digest

**Disorganized Cortical Patches Suggest Prenatal Origin of Autism**

The architecture of the autistic brain is speckled with patches of abnormal neurons, according to research partially funded by NIMH. Published in the *New England Journal of Medicine* on Mar. 27, the study suggests that brain irregularities in children with autism can be traced back to prenatal development.

“While autism is generally considered a developmental brain disorder, research has not identified a consistent or causative lesion,” said NIMH director Dr. Thomas Insel. “If this new report of disorganized architecture in the brains of some children with autism is replicated, we can presume this reflects a process occurring long before birth. This reinforces the importance of early identification and intervention.”

Dr. Eric Courchesne and Dr. Rich Stoner of the Autism Center of Excellence at the University of California, San Diego, joined colleagues from the Allen Institute for Brain Science to investigate the cellular architecture of the brain’s outermost structure, the cortex, in children with autism. Courchesne recently reported an overabundance of neurons in the prefrontal cortex of children with autism. For the current study, the researchers analyzed gene expression in postmortem brain tissue from children with and without autism, all between 2 and 15 years of age.

**Researchers Discover Underlying Genetics, Marker for Stroke, Cardiovascular Disease**

Scientists studying the genomes of nearly 5,000 people have pinpointed a genetic variant tied to an increased risk for stroke and have also uncovered new details about an important metabolic pathway that plays a major role in several common diseases. Together, their findings may provide new clues to underlying genetic and biochemical influences in the development of stroke and cardiovascular disease and may also help lead to new treatment strategies.

“Our findings have the potential to identify new targets in the prevention and treatment of stroke, cardiovascular disease and many other common diseases,” said Dr. Stephen R. Williams at the University of Virginia Cardiovascular Research Center.

Williams and his team reported their findings Mar. 20 in *PLoS Genetics*. The investigators were supported by NHGRI’s Genomics and Randomized Trials Network (GARNET) program.

Stroke is the fourth leading cause of death and a major cause of adult disability in this country, yet its underlying genetics have been difficult to understand. Numerous genetic and environmental factors can contribute to a person having a stroke. The researchers focused on one particular biochemical pathway called the folate one-carbon metabolism pathway.

**Contacts Better Than Permanent Lenses for Babies After Cataract Surgery**

For adults and children who undergo cataract surgery, implantation of an artificial lens is the standard of care. But a clinical trial funded in part by NEI suggests that for most infants, surgery followed by the use of contact lenses for several years—and an eventual lens implant—may be the better solution.

A cataract is a clouding of the eye’s lens and can be removed through a safe, quick surgical procedure. After cataract removal, most adults and children receive a permanent artificial lens, called an intraocular lens (IOL). This is an option for infants, too, but the trial found that the use of contact lenses is safer than, and just as effective as, an IOL for infants under 7 months old. The most recent data from the trial were published Mar. 6 in *JAMA Ophthalmology*.



Child wearing a contact lens

PHOTO: SCOTT LAMBERT, EMORY

“When we began this study, the prevailing theory was that IOLs would be the better option for cataract in infants because they correct vision constantly, while contact lenses can be removed or dislodged from the eye,” said Dr. Scott Lambert, the study’s lead investigator and a professor of ophthalmology at Emory University. “But our data suggest that if the family can manage it, contact lenses are the better option until the child gets older.”

**Sepsis Study of Three Treatments Shows Same Survival Rate**

Survival of patients with septic shock was the same regardless of whether they received treatment based on specific protocols or the usual high-level standard of care, according to a 5-year clinical study. The large-scale randomized trial, named ProCESS (Protocolized Care for Early Septic Shock), was done in 31 academic hospital emergency departments across the country and was funded by NIGMS.

The results of the trial, led by Dr. Derek Angus and Dr. Donald Yealy of the University of Pittsburgh, appeared online Mar. 18 in the *New England Journal of Medicine*.

“ProCESS set out to determine whether a specific protocol would increase the survival rates of people with septic shock,” said Dr. Sarah Dunsmore, who managed the ProCESS trial for NIGMS. “What it showed is that regardless of the method used, patient survival was essentially the same in all three treatment groups, indicating that sepsis patients in these clinical settings were receiving effective care.”

Sepsis is a body-wide inflammation, usually triggered by an infection. It can lead to a dangerous drop in blood pressure, called septic shock, that starves tissues of oxygen and chokes out major organs: lungs, kidneys, liver, intestines, heart. It remains frustratingly hard to identify, predict, diagnose and treat.—compiled by Carla Garnett

# milestones



*Dr. Calbert Laing retired recently as chief of the immunology integrated review group in the Center for Scientific Review.*

## CSR Immunology IRG Chief Laing Retires

By Paula Whitacre

Dr. Calbert Laing still remembers how a headmaster at his primary school in St. Catherine, Jamaica, urged students to aim high throughout life. His message reinforced the major and constant influence of Laing's mother on her children. (Laing is the fifth of nine siblings). She, like others in the community, expected children to be better off than their parents.

"I grew up in a very small hamlet, with no running water, electricity or paved roads," he said. "The one thing we really knew from the time we were little was that education was important. There was no choice."

Laing retired recently as chief of the immunology integrated review group (IRG) in the Center for Scientific Review. He oversaw the work of about 10 scientific review officers (SROs) and assisted in many special efforts in his 26-year career at NIH. For example, he helped coordinate review of applications for Bridges to the Future. He received three NIH Director's Awards and one DHHS award, as well as several CSR awards.

"One of the most remarkable things about Cal is that he is an extremely good mentor," said Dr. Seymour Garte, director of the Division of Physiological and Pathological Sciences. "Many of the present senior leadership, including other chiefs and division directors at CSR, came from his mentorship."

Dr. Alexander Politis joined CSR in 1998 with Laing as his first supervisor. Politis credits Laing's emphasis on "philosophy and principles anchored in peer review concepts and fairness" in forming his own career as an SRO and now chief of the infectious diseases and microbiology IRG. "He was so consistent, so right on the spot," said Politis. "Since I've been a chief, I have trained many SROs and I go back to how Cal taught me."

After graduating first in his class in secondary school, Laing worked as an administrator on a sugar plantation and in agricultural marketing. At age 25, he entered Tuskegee Institute (now University) as a freshman and graduated *summa cum laude* with a B.S. in biology.

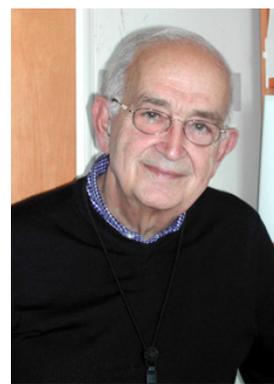
Laing earned his Ph.D. in biology with a concentration in immunology from Brown University

in 1974 and conducted postdoctoral research at Mt. Sinai Medical Center. His research centered on the isolation and characterization of antigens from the mammary tumor of the mouse.

While in New York, he taught biology at the Fashion Institute of Technology. From 1977 to 1987, Laing served on the faculty of Howard University College of Medicine, rising to the rank of associate professor with tenure, and received two substantial NIH grants on his first attempts.

"I had an idea that I wanted to accomplish something else, but couldn't define what I was looking for," he said. When he saw an announcement for executive secretary (now SRO), he realized the NIH position was the right career change. He joined NIH in 1987 and became immunology IRG chief in 1998.

Laing plans to stay in the Washington, D.C., area, but his connections to Jamaica remain strong. He hopes to complete a memoir, recounting such adventures as traveling to a town several hours away—by himself, at age 11—to pick up a calf won through the 4H Club. An avid cook and gardener, he plans to bring to market a Jamaican jerk sauce, based on his own recipe. As his former headmaster and his beloved "Mommy" urged, Laing achieved much during his career and will continue doing so during retirement.



## NIAID's Kapikian Mourned

Dr. Albert Z. Kapikian, a pioneering virologist at NIAID who discovered norovirus and led a decades-long effort that resulted in the first licensed rotavirus vaccine, died on Feb. 24. He was 83 years old. Kapikian

was former chief of the epidemiology section of NIAID's Laboratory of Infectious Diseases (LID), a position he held for 45 years.

"Al Kapikian was a giant in the field of virology," said Dr. Anthony Fauci, director of NIAID. "His seminal basic and clinical research contributions to the study of viruses and to vaccine development have had an enormous global impact. Importantly, he was a warm-hearted, beloved and widely respected human being. His many friends at NIAID and NIH mourn the loss of their esteemed colleague."

Kapikian often was called the father of human gastroenteritis virus research for his work on

improving the understanding and prevention of viral diseases that affect the gastrointestinal tract. In 1972, he identified the first norovirus, initially called Norwalk virus. Noroviruses are now recognized as a major cause of epidemic diarrhea in adults worldwide. In 1973, Kapikian and his colleagues identified the hepatitis A virus. He also was the first scientist in the United States to detect human rotavirus, which had been discovered by others in Australia. He dedicated himself to studying this leading cause of severe diarrhea in children, which accounts for more than 400,000 deaths annually, mostly in developing countries.

“Al was my hero,” said Dr. Kathryn Zoon, director of the NIAID Division of Intramural Research. “He was a modest man who made many remarkable discoveries in virology and saved many lives through his vaccine development efforts. He will be missed by his NIAID family.”

Kapikian and his research group defined the mode of transmission of rotavirus, identified the viral proteins critical for triggering an immune response and formulated a vaccine that targeted several important rotavirus strains. These efforts ultimately led to the development, testing and approval by the Food and Drug Administration in 1998 of the first rotavirus vaccine. Subsequently, Kapikian headed the development of second-generation rotavirus vaccines that have been licensed by pharmaceutical companies in Brazil, China and India. He also contributed to ongoing efforts to improve rotavirus vaccines and expand their use in the developing world.

“Al Kapikian was a close and highly valued friend and colleague for the more than 50 years we served together in the Laboratory of Infectious Diseases,” said Dr. Robert Purcell, former chief of LID’s hepatitis viruses section. “His strengths were a keen and inquiring mind, buttressed by scrupulous honesty and respect for scientific truth. One of his greatest scientific triumphs, the development of the first rotavirus vaccine, continued to motivate him through and even after retirement, not for personal prestige or financial gain, but because of the high death rate of rotavirus-infected infants and children. To him, the control of rotavirus disease was a personal responsibility. These and his many other qualities made him a friend of all.”

Kapikian, of Armenian heritage, grew up in Brooklyn. He received his medical degree from Cornell University Medical College in 1956 and joined NIAID in 1957. His numerous accomplishments earned him the Albert B. Sabin Gold

Medal, the Maurice Hilleman/Merck Award of the American Society for Microbiology and the Children’s Vaccine Initiative Pasteur Award, among many other honors.

Kapikian is survived by his wife, Catherine—whom he met at the NIH medical arts department—three sons and two grandchildren.

### NIDCR Mourns McCartney-Francis

Dr. Nancy McCartney-Francis, an immunologist at NIDCR, died Jan. 24 at age 63 in North Potomac from complications of systemic lupus erythematosus. She had served for nearly 30 years in NIDCR’s Oral Infection and Immunity Branch and for the past 2 years in the Craniofacial and Skeletal Diseases Branch.

“For those of us who had the privilege of knowing Nancy and working with her, she will be sorely missed,” said Dr. Sharon Wahl, NIDCR scientist emeritus. “In addition to her scientific achievements, Nancy will be remembered for her beautiful smile, her musical gifts, her quiet tenacity and her friendship.”

McCartney-Francis received her undergraduate degree from the University of Kansas, where she graduated Phi Beta Kappa. She earned a master’s degree in microbiology at the University of Texas, where she also obtained her Ph.D. in microbiology in 1980.

She served as a postdoc from 1981-1985 in the laboratory of NIAID’s Dr. Rose Mage, an expert in immunochemistry, immunogenetics and molecular immunology.

In 1985, McCartney-Francis joined what was then NIDR’s Laboratory of Immunology under the direction of Wahl; she worked there for almost 30 years. She joined the Craniofacial and Skeletal Diseases Branch when Wahl retired.

Much of McCartney-Francis’s research focused on TGF-beta and immune function, inflammation and mechanisms of host defense with special relevance to autoimmune diseases. She also served as a mentor to many—training, assisting and supporting investigators and students.

“Nancy was a superb and inspiring mentor, being patient and kind while instilling students and fellows under her watchful eye with her passion for scientific inquiry, technical expertise, excellence, honesty and—importantly—excitement for good data,” said Wahl.

McCartney-Francis received numerous honors and awards, including a special commendation from Georgetown University Medical Center for her continued participation in its M.S. in Biochemistry and Molecular Biology Intern Program. Other honors included those from the American Cancer Society, a NRSA award, a NIAID Special Achievement Award, a NIDR Scientific Director’s Award and multiple performance awards.

“Nancy was a true team player and galvanized those around her,” said Wahl. “Beyond her life in science, she had a passion for service and community and was actively involved in her church where she was a remarkably talented organizer and a source of vision and action.” She also loved art, craft fairs and all forms of music.

McCartney-Francis was predeceased by her husband and parents. 



## Circus Premiere Night Cheers Youngsters, Families

For the 17th year, the NIH Recreation and Welfare Association provided a memorable night on Mar. 19 for the NIH community, patients and a variety of social service programs in the D.C. metro area. R&W was able to treat more than 2,500 children and their families to the annual Premiere Night of Ringling Bros. and Barnum & Bailey Circus at the Verizon Center.

The children come from social service agencies, where an evening out for entertainment normally does not occur. Besides the Children's Inn at NIH and Special Love, youngsters came from Bethesda Cares, Family Shelters, Operation Second Chance, Children's National Medical Center, as well as patients from Georgetown and Howard University.

R&W shares the evening with Easter Seals and its clients—a total of 11,000 tickets were purchased for the event. This year, Friends of the Clinical Center funded a pre-circus pizza party for families from NIH.

The evening, with a theme of "Built to Amaze," did just that, said R&W President Randy Schools. "Many emails came to the R&W, appreciating the opportunity to be part of the event," he added. "On behalf of the charities who were able to attend, a special thanks goes out to all who participated. We hope you will join us for this special evening again next year."



**Above:**

*Clinical Center patient Kristen Wells finds out that laughter is indeed a medicine. At right, CC patient Diamond Kemp gets a visit by circus clowns. The visit was arranged by R&W and included stops at the Children's Inn at NIH and a special party where clowns entertained families at Verizon Center.*

**Below:**

*At left, CC patient Felix Rojasreynoso and his mother Sandra Reynoso Garcia enjoy the company of Boss Clown (l) and Oscar. The two clowns visited the CC's 1N/W/DH pediatric unit on Mar. 19. At right, having fun at the pre-circus pizza party are (from l) Heather Alba, Samantha Bentley and Amy Alba, part of a Special Love program called "Some Day I Will Join the Circus."*



*Above, family members of a CC patient join up with circus celebrities. At right, Dave Smith, president of Special Love, Inc., and his son Willie make believe they are in the circus.*

*Left, friends and families associated with Special Love, which runs Camp Fantastic each August, were guests at the circus.*

PHOTOS: MICHAEL SPENCER, ERNIE BRANSON