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MARCH 2, 2012

The Second Best Thing About Payday

Atala Surveys Successes of Regenerative Medicine

By Rich McManus

Just as the auto parts store is a boon to the car repair business, the field of regenerative medicine is slowly becoming an invaluable parts warehouse as thousands of scientists from many fields including cell biology, engineering and physics are collaborating to build facsimiles of human tissues, structures and organs.

Already, there is a college student named Luke M. who, a decade ago, received a hand-crafted bladder and has been living a largely normal life, said Dr. Anthony Atala, who gave a Wednesday Afternoon Lecture on Jan. 25 titled, "Regenerative Medicine: Current Concepts and Changing Trends."

Director of the Wake Forest Institute of Regenerative Medicine at Wake Forest Baptist Medical Center, he surveyed the problems and promise of a field that can be traced back at least as far as the first human organ transplant, a kidney, in Boston in 1954. A quarter century before that, the book *The Culture*



Dr. Anthony Atala speaks at NIH.

SEE ATALA, PAGE 6



NHLBI acting director Dr. Susan Shurin and acting deputy director Dr. Carl Roth express their thanks.

On National Wear Red Day

NIH Expresses Thanks via Flash Mob

NHLBI honored those who work to advance heart disease research and care on National Wear Red Day on Feb. 3, with more than 70 NIH staff members performing a flash mob dance in front of surprised Clinical Center patients and staff.

SEE FLASH MOB, PAGE 4

NINR Director's Lecture Features Commitment to Reducing Infections

By Andria Cimino

"What is the evidence that there is any relationship between hand-washing and infection?" This question served as a wake-up call to critical care nurse Elaine Larson, who in the late 1970s worked in an ICU where many patient-staff interactions were not followed by hand-washing. At the end of a 2-year study, Larson and an epidemiologist colleague observed that providing additional hand-washing facilities "was not associated with reduced nosocomial acquisition of organisms or improved hand hygiene."

Nosocomial infections, also known as health care-associated infections or HAIs, are a serious public health concern. They are the most common complication of hospital care and are one of the top 10 leading causes of death in the U.S. Yet nearly 150 years after Hungarian physician Ignaz Semmelweis instituted hand-washing to prevent puerperal fever in his obstetrical ward, reducing the mortality rate



briefs

STEP Forum on Sleep, Mar. 13

The staff training in extramural programs (STEP) committee will present a Science for All forum on the topic "I'm not aSLEEP...But That Doesn't Mean I'm Awake," on Tuesday, Mar. 13, from 9 a.m. to noon in Rockledge II, Rms. 9112-9116.

How much sleep do you really need? We all know people who seem to need only 4 or 5 hours of sleep, but are they functioning at an optimal level? Sleep affects every aspect of your life—mood, emotions, memory, physiology and public safety. Join us to learn about the latest scientific findings on sleep, sleep impairment, long-term effects of sleep deprivation and treatment strategies.

Goodbye Bottled Water, Hello Fountains

The Office of Research Facilities has begun removing bottled water dispensers from certain locations on campus. The affected dispensers are near water fountains that were previously out of service, but have since been repaired or replaced. The bottled water dispensers will remain in buildings or locations where the water supply has been determined to be unhealthy or not available. If you have questions or concerns, contact the facility manager for your building.

Circus Premiere Night Benefits Charities

The 15th annual Children's Premiere Night with Ringling Bros. and Barnum & Bailey Circus will once again benefit the NIH children's charities. The 141st edition of "The Greatest Show on Earth" comes to Verizon Center on Wednesday, Mar. 14, hosted by the NIH R&W. A free pre-show starts at 6 p.m. and the circus starts at 7. Tickets include Circus Celebrity—front row/interactive seating where you become part of the show \$80 (reg. \$110); front row \$55 (reg. \$75); VIP \$40 (reg. \$55); section 111 & 112 (best seats) \$24 (reg. \$35). Purchase your ticket at the R&W activities desk in Bldg. 31, Rm. B1W30 or call (301) 496-4600. Orders can be placed for tickets at any R&W store.

Orioles and Nationals Baseball Ticket Sales

The R&W will once again offer tickets to the Baltimore Orioles and Washington Nationals. Orioles tickets go on sale Tuesday, Mar. 6 in Bldg. 31, Rm. B1W30 (outside the R&W gift shop) at 8 a.m. Available are two regular season tickets (2 seats behind first base—section 14BBB seats 7-8). Nationals tickets go on sale on Thursday, Mar. 8 outside the Bldg. 31 R&W

gift shop, also at 8 a.m. R&W has 2 seats in section 219, row D. You must be a 2012 R&W member to buy tickets. Membership is \$7 for the year and can be purchased at the same time you get tickets.

Campus Bluebird Houses Seek Monitors

Volunteers are needed to help monitor bluebird houses on campus. "Monitoring will begin about Apr. 1 and end about Aug. 10," said Lynn Mueller, landscape architect, Office of Research Facilities. "We have eight trails surrounding the campus with 10 to 12 houses each."

Volunteers would take a weekly lunch-time walk along the trail looking for bluebirds, inspecting boxes, counting eggs and babies and noting when and how many babies mature and fly away. A second nesting begins in late June. Each trail will have a team of 3 to 4 volunteers so individuals will not have to make every weekly tour.

"The campus bluebird population is making a nice comeback from the recent West Nile virus outbreak, with 36 bluebirds that fledged in 2011," Mueller noted. "Many other songbird species use the nest boxes as well."

If you are interested in helping monitor bluebirds this season, contact Mueller at muellerl@mail.nih.gov or (301) 594-7699.

Reddy Joins NIGMS

Dr. Michael "Mike" Reddy recently joined NIGMS as program director in its Division of Genetics and Developmental Biology. He will administer research grants on DNA replication and postdoctoral fellowship grants in the areas of genetics and developmental biology. Before coming to NIGMS, Reddy was a scientist in the planetary sciences division at NASA headquarters. Prior to that, he did a 2-year rotation as a program director in the National Science Foundation's division of molecular and cellular biosciences. Earlier, he was a faculty member for 15 years in the chemistry and biochemistry department at the University of Wisconsin-Milwaukee. Reddy earned a B.A. and M.A. in biology from the State University of New York at Buffalo and a Ph.D. in molecular microbiology from SUNY-Stony Brook. His postdoctoral research was in the laboratory of Peter von Hippel at the University of Oregon.



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NIH...Turning Discovery Into Health

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Dr. Wanda Whitten-Shurney discusses the legacy of her father, Dr. Charles Whitten.

Daughter Pays Tribute Sickle Cell Pioneer Whitten's Papers Come to NLM

By Dever Powell

How do you tell the story of an accomplished polymath—pediatric hematologist, co-founder of the Sickle Cell Disease Association of America (SCDAA), father—who advanced science, education and outreach for sickle cell disease? One way: through his papers.

"My first name is Wanda, but my last name is Dr. Charles Whitten's daughter," said Dr. Wanda Whitten-Shurney, pediatrician at the comprehensive sickle cell clinic at Children's Hospital of Michigan and CEO and medical director of SCDAA's Michigan chapter. "I stand firmly on his shoulders."

NLM director Dr. Donald Lindberg welcomed an audience that included Whitten family members and SCDAA President Sonja Banks to Lister Hill Auditorium on Feb. 2 to hear Whitten-Shurney's tribute to her father, illustrated through his papers. "On this occasion, we are able to thank the Whitten family most sincerely for the gift of the papers," Lindberg said. The gift was first announced at the 2010 NIH James B. Herrick Symposium: Sickle Cell Disease Care and Research.

Whitten-Shurney shared her struggle to condense her father's life into a 45-minute talk. Whitten did so many things, for so many people, in so many different spheres.

The talk, "Introducing Charles Whitten: Scientist, Humanitarian, Family Man," illustrated Whitten's landmark work fighting SCD.

In sickle cell anemia, the body produces crescent or sickle-shaped red blood cells, resulting in anemia. The sickle cells also get stuck in blood vessels, blocking blood flow, increasing risk of infection and causing excruciating pain and organ damage.



Whitten-Shurney (l) poses with (from l) NLM director Dr. Donald Lindberg, widow Mrs. Eloise Culmer Whitten and Dr. Lisa Whitten.

PHOTOS: MICHAEL SPENCER

People with SCD are born with two sickle cell genes, one from each parent. A person with sickle cell trait, or one sickle cell gene, doesn't have the disease but can pass it on. Most states test newborns as part of their screening programs. Whitten-Shurney said her father was among the first to insist on and to develop newborn screening for SCD, which is now performed worldwide.

Education was paramount to Whitten. Whitten-Shurney described one innovative example: the Whitten dice. "Most men find out they have sickle cell trait only after they have a baby with SCD," she said. One in 12 African Americans carries the trait. Whitten developed color-coded dice to educate couples about genetic risks. This was one of many methods he used to promote SCD awareness.

Whitten also made a lasting contribution to medical education: Wayne State University's post-baccalaureate enrichment program. "This program led to more African Americans in a medical school [Wayne State] than any other school besides Howard," Whitten-Shurney said.

The Whitten papers include letters from former students and photographs of his philanthropic outreach with the SCDAA, a network that has included Muhammad Ali, Diahann Carroll, Ruby Dee and Ossie Davis and Archbishop Desmond Tutu. The papers also tell the story of Clinique Whitten, an SCD clinic in Haiti.

Whitten-Shurney devoted the final moments of the talk to portraying her dad as a family man. Despite all the time he spent bettering the world, Whitten was always there for his family. Among his favorite pastimes was baking chocolate cake. At the end of the lecture, Whitten-Shurney handed out copies of a chocolate cake recipe, a fitting tribute for the occasion.



FLASH MOB

CONTINUED FROM PAGE 1

Above:

On Wear Red Day, Feb. 3, NIH staff gathered to thank those who work to advance heart disease research and clinical care every day.

Below:

A few of the personal heart-related messages written for a table display on Wear Red Day

For 10 years, NHLBI has led the nation in observing National Wear Red Day—an opportunity to raise awareness that heart disease, while still the #1 killer of American women and men, is largely preventable.

This year's event was intended to "thank the incredible teams—scientists, doctors, nurses, clinical trial participants, educators, volunteers and many others across the country—who are working to advance heart disease research and clinical care every day," said NHLBI acting director Dr. Susan Shurin, who participated in the flash mob.

During the 4-minute performance, staff danced to Lulu's cover of *Put a Little Love in Your Heart* and held up thank-you signs before urging onlookers to join in the fun.

A table display next to the performance area encouraged passersby to write personal messages about heart health in paper hearts and to pick up educational materials.

Videos of the flash mob were posted on the NHLBI and NIH YouTube channels and were promoted through social media to get the word out to those who work beyond campus as well as to staff who did not attend. The videos racked up a combined total of more than 5,000 views within the first 2 weeks.

The flash mob was one of many activities led by NHLBI during American Heart Month in February. The 10th annual Red Dress Collection 2012 showed at Fashion Week in New York City on Feb. 8, with 17 celebrities walking the runway in awareness-raising designer red dresses. NHLBI staff joined the Mayo Clinic and WomenHeart on a panel discussion for members of the media, highlighting progress and reflecting on challenges still facing the women's heart health movement.

NHLBI also continues to partner with HHS's Million Hearts to prevent 1 million heart attacks and strokes over the next 5 years.

Watch the flash mob video on the Director's Corner link at <http://www.nhlbi.nih.gov/> and share it with others to continue to spread the message of thanks.





Dr. Robert M. Califf of Duke University

Duke's Califf Addresses Clinical Trials, Mar. 8 in Bldg. 45

Dr. Robert M. Califf, vice chancellor for clinical research, director of Duke Translational Medicine Institute and professor of medicine at Duke University Medical Center, will speak on "Innovative Approaches to Clinical Trials," on Thursday, Mar. 8, from 10 a.m. to noon in Bldg. 45, Rms. E1-E2.

With the science of clinical trials evolving quickly, Califf will discuss the role and value non-randomized controlled trials have in medical research and clinical trials. The number of therapeutic interventions is growing and the need for clear scientific evidence that these interventions work is mounting. Recent emphasis on evidence-based medicine, patient-centered outcomes research, learning and accountable health care systems underscores the fact that most clinical trials fail to provide the evidence needed to inform medical decision-making. The need for a balance between commercial interests and public health is warranted.

In addition to his faculty appointments at Duke, Califf is editor-in-chief of *American Heart Journal* and is the author or coauthor of more than 1,000 peer-reviewed articles. He also serves as a contributing editor for www.theheart.org, an online information resource for health care professionals involved in the diagnosis and management of cardiovascular disease.

Califf received his undergraduate degree from Duke and his M.D. from Duke University Medical School.

The seminar is sponsored by the Office of Disease Prevention and several institutes. Registration is not required; seating is on a first-come, first-served basis. Sign language interpreters will be provided. For reasonable accommodation, contact Paris Watson at [\(Paris.Watson@nih.gov\)](mailto:Paris.Watson@nih.gov), (301) 496-6615.

Intervention Could Save Lives Grief Can Bring on Heart Attack, Grantees Show

Researchers at Beth Israel Deaconess Medical Center and Harvard School of Public Health have learned that newly grieving or bereaved individuals are at 21 times the normal risk of a heart attack in the first 24 hours following the loss of a significant person. Although this risk drops over time, after a week it is still greatly elevated and even after a month the risk remains well above average, the NIH-supported investigators have shown.

Results from the Determinants of MI Onset Study were published in the American Heart Association's journal *Circulation*. The work was funded by NHLBI and NIAID.

The researchers interviewed some 2,000 cardiac patients, all of whom were in the hospital for a heart attack. Findings revealed that while the overall risk for heart attack (myocardial infarction or MI) was greatest over the first 24-hour period following the loss, there was still an 8-fold likelihood of MI occurrence a week after the death of a significant social contact. After a month, that number was halved. Overall, 270 people experienced a heart attack within 6 months of the loss of another, while 19 people had lost a close acquaintance or loved one the day before having an MI.

The findings hold clinical implications for the bereaved, their family members and health workers, according to lead investigator and epidemiologist Dr. Elizabeth Mostofsky.

In terms of stressful life events, the death of a family member or close acquaintance ranks high. The loss of a spouse ranks first, according to the Holmes-Rahe Life Stress Inventory, well ahead of the second leading stressor, divorce. The loss of another family member rates fourth.

It is well documented that adverse stress, especially abrupt or acute stress, can have detrimental effects on both mind and body, provoking various somatic (bodily) complaints (headache, muscular tension and discomfort, stomach ailments, etc.). Until now, however, there have been no studies to examine the acute effects of bereavement on MI risk.

A survivor's life can be turned upside down after the loss of a spouse or significant other. Following the loss, the survivor "may experience feelings of depression, anxiety and anger, stressors that may lead to physiologic sequelae such as higher blood pressure and heart rate and more blood clotting that increase the risk of a heart attack," noted Mostofsky.

What stood out prominently in the study was the robust nature of the findings, in particular that the effects were so dramatic and can occur so quickly following an individual's loss, according to the scientists.

"Here is an opportunity for family members and clinicians to intervene and make a difference," Mostofsky said. The take-home message? "It is very important that bereaved individuals take special care of themselves during the grieving process. For instance, they [and their supporting family members] should make sure to take their medicines and get ample rest," she concluded.—**Jan Ehrman**

ATALA

CONTINUED FROM PAGE 1



Atala offered glimpses of technologies on the horizon that will make today's breakthroughs such as artificial bladders look like the iron lungs of yesteryear.

PHOTOS: MICHAEL SPENCER

of *Organs* had been published, with famed aviator Charles Lindbergh as a coauthor.

"There have been many advances since that time, and so many lives have been saved," said Atala, but shortages of human organs and the stubborn problem of transplant rejection remain major obstacles.

Back in 1981, the first use of a patient's own cells for regenerative therapy took place at Massachusetts General Hospital, in a burn victim, Atala said. Scientists expanded a population of skin cells and introduced them to the patient. The cells did not generate new skin, but they did enhance the healing process.

"Why have there been so few clinical advances?" Atala asked, before enumerating three main challenges to the field: an inability to grow desired populations of cells *in vitro*, inadequate biomaterials and inadequate vascularity, or blood flow.

But even these hurdles are being surmounted in recent decades, owing to major advances in the biology of growth factors, Atala said.

The discovery of progenitor cells has been the key to cell expansion outside the body, he explained.

"Within 60 days, we can take a cell line the size of half a postage stamp and grow enough cells to cover a football field," he said. "Most cell types can, in fact, be grown and expanded outside the body, with the exception of liver, nerve and pancreas. For those we need stem cell populations."

A urologist by training and head of Wake Forest Baptist's urology department, Atala demonstrated a host of clinical advances focusing, unsurprisingly, on mid-body organs and tissues. No matter what they are trying to replicate—urethra, bladder, vagina, penis—his team follows a basic strategy: begin with human cell populations, seed polymer scaffolds with the cells, test the implants in mice and rabbits, then conduct post-implant analyses before proceeding to human trials.

The field recognizes four levels of regenerative complexity. Level 1 is flat tissue such as skin, which is the simplest to recreate, Atala said. Level 2 is tubular structures such as blood vessels. Level 3 is hollow, nontubular structures; bladders are an example. Level 4, solid organs, "is by far the most complex—there is a massive need for vascularity."

One of Atala's first targets for repair was the urethra. In 1996, he and colleagues used a piece of biomaterial comprised of the extracellular matrix

from pig bladder and placed it over a urethral defect—in effect creating a bridge that cells could grow across. The scientists took advantage of the insight that, as long as the installed matrix was no further than one centimeter from an edge of healthy tissue, the assimilation would succeed.

But what if the defect is larger than 1 cm? Just last year, Atala's team reported in *The Lancet* the successful creation of a new urethra built with a biodegradable scaffold and a patient's own cells that restored structure and function to the patient.

Atala's institute has gone on to create blood vessels, heart valves and vaginal organs. Engineered bladders have been implanted in spina bifida patients.

"These constructs appear to be doing well as patients get older and grow," Atala reported of work that has been ongoing for 14 years.

In a penile replacement project undertaken in rabbits that began first as partial then full replacement, the proof was in the pudding—impregnated bunnies gave birth to healthy offspring; the work was reported in 2010 in the *Proceedings of the National Academy of Sciences*.

Interestingly, the processes of both vascularization and innervation, or nerve growth, require about half a year for the process to be complete, Atala noted.

He offered glimpses of technologies on the horizon that will make today's breakthroughs such as artificial bladders look like the iron lungs of yesteryear: there are "bioprinters" resembling inkjet printers that lay down thin layers of cells to create two-chambered hearts; cell-rich wafers can be inserted into animals' kidneys to restore function. Scientists at the University of Paris are using amniotic and placental stem cells to repopulate the bone marrow, he said, a prospect he called "very exciting."

Therapies relying on cells alone represent the grail of regenerative medicine. Atala thinks that a shrewd enough harvest of stem cells from normally discarded afterbirth could potentially supply 99 percent of the U.S. population's need for such cells.

"Five years ago, we couldn't get heart cell populations to expand outside the body, but now it is possible," he said. "But it's not all about advances in cell biology, or the type of cells we choose...it's all about making patients better," he concluded. ☐

feedback

Wondering about some aspect of working at NIH? You can post anonymous questions at www.nih.gov/nihrecord/index.htm (click on the Feedback icon) and we'll try to provide answers.

Feedback: Isn't telework being pushed upon us due to an executive-level mandate? Agencies can now post end-of-year accomplishments of high levels of teleworkers. I was told that I have to take 2 days each pay period to telework! Clinical staff, researchers, maintenance and food service will not have that luxury. I imagine robotics to remove snow would be of great interest. Are supervisors actually going to spend time to review what work has been accomplished while the staff person sits at home? Here's hoping that this is also a mandate.

Reply from the Office of Human Resources: In December 2010, legislation was passed and signed by the President that provides agencies greater flexibility to manage their workforce. It allows agencies to maximize the use of flexible work arrangements for recruiting and retaining valuable talent, maintaining operations during emergencies, improving management efficiencies and promoting initiatives that enhance the work-life balance of employees.

NIH has taken major steps, based on that legislation and the impacts of BRAC on traffic around campus. These include determining the eligibility of all employees to participate in telework, establishing a workgroup of IC and Office of Management leadership to guide trans-NIH efforts to enhance telework and flexible work schedules as workforce management and environmental sustainability tools, examining barriers and challenges that might hinder more widespread use of telework and sponsoring a telework festival to increase awareness of those flexibilities.

NIH has seen a 70 percent increase in teleworkers over the previous year as a result of these efforts. In response to the question about supervisors reviewing work done by teleworkers, yes, they will be spending time on that, just as they do now whether the employee is at home teleworking or is in the office.

OHR provides training that managers and teleworkers take before establishing an arrangement. It emphasizes two key principles: first, obligations and responsibilities don't change based on where work is performed and second, supervisors should manage by results. The significance of selecting individuals for telework who perform well in the office is evidenced by reports from employees that they're able

to focus better and get more done in a shorter time while teleworking, facts that are confirmed by their supervisors. The performance elements of the PMAP don't change and neither do the oversight requirements of supervisors for employees who work at home or in the office. The new telework agreement emphasizes that point by requiring employees to complete all work assignments in accordance with guidelines, standards and metrics stated in their performance plan and/or as indicated by their supervisor.



Feedback: Why doesn't NIH have a uniform telework plan? Some ICs get to telework 3 days a week (or more) while others [are permitted] only 1 day a pay period. We are told the 1 day a pay period is because some of us are on AWS. We believe this is not in the spirit the President had when he [signed] the Telework Improvement Act in 2010. All of us should be treated equally no matter what IC we work in. With gasoline up to \$3.70 a gallon and with all the traffic around campus, not to mention parking [problems], having a uniform telework plan in place makes sense. If you want an example of a great telework plan, look no further than GSA.

Response from OHR: There is an NIH-wide telework policy; it's available at <http://oma.od.nih.gov/manualchapters/person/2300-600-1>. One of the most important aspects of telework, determining the eligibility of employees and duties, is usually done at the supervisory level so the IC role of creating internal guidance is critical for ensuring the program is implemented fairly and equitably. Within that framework, managers and supervisors generally have discretion to implement telework to fit the business needs of their organizations. The criteria about business needs are a crucial component of the decision-making process and supervisors in the IC are in the best position to make workplace and telework determinations.

New Geroscience Interest Group Meets, Mar. 8

"Aging underlies everything. If we can understand what's happening in the aging cell, we will have a key to treating a host of chronic diseases that come with growing older." So says Dr. Felipe Sierra, director of NIA's Division of Aging Biology and a moving force behind the new trans-NIH geroscience interest group (GSIG). The goal of the group is to stimulate interest and involvement in the basic science of aging across ICs at NIH; it has been launched with the blessing of a number of IC directors.

The group's first NIH-wide effort is a seminar series on aging and disease topics. The first speaker will be Dr. James L. Kirkland, director of the Robert and Arlene Kogod Center on Aging at the Mayo Clinic, who will discuss cell senescence and other aging topics on Thursday, Mar. 8. The seminar, "Targeting Aging to Delay Multiple Chronic Diseases: A New Frontier," will take place in Masur Auditorium at 11:30 a.m. Kirkland will expand on his recent article in *Nature*, which described a causal relationship between senescent cells and certain age-related diseases in a mouse model. Two additional seminars are planned for later this year, as well as a workshop on the topic of inflammation and age-related diseases. The GSIG also sponsors a journal club that meets monthly.

"Aging is the major risk factor for most chronic diseases," says Sierra. "The good news is that it's a malleable factor. By decelerating aging we should be able to change or reduce the risk for many diseases in unison. But we need to understand the basic molecular, cellular and genetic mechanisms involved and how they change as we age." For more information about GSIG, contact Sierra at sierraf@nia.nih.gov.

INFECTION CONTROL

CONTINUED FROM PAGE 1

to less than 1 percent, Larson found that hand-washing as a primary infection prevention strategy was still disregarded by members of the health care community.

At the second annual NINR Director's Lecture, "Infection Prevention: An Interdisciplinary Team Approach," Larson, now associate dean for research and professor of pharmaceutical and therapeutic research at Columbia University School of Nursing, professor of epidemiology at Columbia's Mailman School of Public Health and director of Columbia's Center for Interdisciplinary Research to Prevent Antimicrobial Resistance (CIRAR), discussed her career-long effort to build an evidence base that would help identify, prevent and control infection. "We knew HAIs were common, but the question was how preventable were they?"

In her early studies, Larson sought to determine what organisms colonized the hands of health care professionals, track caregivers' hygiene practices and see if there was a correlation between these variables and the rate of HAIs among patients. When she realized the skills needed to answer these questions exceeded her clinical experience, Larson found collaborators, putting together an interdisciplinary team that included a surgeon, an epidemiologist, nursing staff and administration, a microbiologist, a statistician and a dermatologist.

Her team's findings—that ICU staff persistently carried one or more of 22 species of gram-negative bacteria even after washing; that 21 percent of 541 HAIs contracted over a 7-month period were caused by species found on staff hands; that less than half of the staff routinely washed their hands following contact with infected patients—firmly established a causal link. When they looked at differences in colonization rates by discipline they found that while physicians had higher counts than nurses, nurses had a greater percentage of antimicrobial-resistant flora. This was "very concerning because the colonizing flora remained with staff over time; this wasn't a transient event," Larson explained.

These early studies laid the foundation for interventional trials to examine the best methods not only for washing hands, but also for convincing health care staff of the need to do so. She added new collaborators with expertise in psychology,

sociology, clinical trials and infectious disease medicine. With the release of the *CDC Hand Hygiene Guidelines* in 2002, which called for the use of alcohol products rather than soap and water, "a panacea, we thought—no sinks, no drying, cheap and easy," Larson thought her work was done. But after conducting site visits at 40 U.S. hospitals that participate in the National Nosocomial Infections Surveillance reporting system to assess the impact of the guidelines, she found that hand hygiene rates had not budged since her first study in 1983. Although nearly 90 percent of the 1,359 ICU nurses observed were familiar with the guidelines, the mean rate for hand-washing remained at 56 percent.

Larson realized that she must change her focus from individual to cultural and systemic factors. Her research team diversified again as she added experts in systems theory, organizational change, industrial engineering and economics. She also developed key relationships with other stakeholders in the fight against infectious diseases, including representatives from the New York City health department, CDC, WHO, FDA, EPA, JCAHO, professional organizations, the media and even a soap manufacturer.

In the past decade, Larson's efforts have targeted practice standards, policy and education. In 2004, she established CIRAR, which teaches interdisciplinary research methods to prevent and control infections and develops behavioral and systems interventions that "make it easier to do the right thing." She also helped write the *2009 WHO Guidelines for Healthcare Personnel Hand Hygiene*, which presents a new approach for teaching hand hygiene.

In closing, Larson shared her motivation to eradicate HAIs, showing the pictures of children she had known who were perfectly healthy, but died from MRSA infections. She noted that in an era in which antibiotic resistance is growing and few new ones are being developed, "we must depend on behavior."

NINR director Dr. Patricia Grady presented Larson with the Director's Lecture award, stating, "Dr. Larson's extremely important research guides practice and fuels the development and dissemination of knowledge across the globe. Her approach for conducting innovative and highly effective team science and for informing her research with practice-based evidence epitomizes what we at NINR, as well as nurse scientists across the globe, do best."

The NIH videocast of Larson's presentation is available at <http://videocast.nih.gov/summary.asp?Live=10942>.



NINR director Dr. Patricia Grady (l) presents Dr. Elaine Larson with the 2012 NINR Director's Lecture Award.

PHOTO: BILL BRANSON

High Levels of Cadmium, Lead in Blood Linked to Pregnancy Delay

Higher blood levels of cadmium in females, and higher blood levels of lead in males, delayed pregnancy in couples trying to become pregnant, according to a study by researchers at NIH and other academic research institutions.

Cigarette smoke is the most common source of exposure to cadmium, a toxic metal found in the Earth's crust that is used in batteries, pigments, metal coatings and plastics. Smokers are estimated to have twice the levels of cadmium as do non-smokers. Exposure also occurs in workplaces where cadmium-containing products are made and from the air near industrial facilities that emit cadmium. Airborne cadmium particles can travel long distances before settling on the ground or water. Soil levels of cadmium vary with location. Fish, plants and animals absorb cadmium from the environment and all foods contain at least low levels of the metal.

Lead, a toxic metal also found in the Earth's crust, is used in a variety of products such as ceramics, pipes and batteries. Common sources of lead exposure in the U.S. include lead-based paint in older homes, lead-glazed pottery, contaminated soil and contaminated drinking water.

Exposure to these metals is known to have a number of effects on human health, but the effects on human fertility have not been extensively studied, especially when studying both partners of a couple. The study was published online in *Chemosphere*. The study's principal investigator was Dr. Germaine M. Buck Louis of NICHD.

"Our results indicate that men and women planning to have children should minimize their exposure to lead and cadmium," Buck Louis said. "They can reduce cadmium exposure by avoiding cigarettes or by quitting if they are current smokers, especially if they intend to become pregnant in the future. Similarly, they can take steps to reduce their exposure to lead-based paints, which may occur in older housing, including during periods of home renovation."

Autoinjectors Offer Way to Treat Prolonged Seizures

Drug delivery into muscle using an autoinjector, akin to the EpiPen used to treat serious allergic reactions, is faster and may be a more effective

way to stop status epilepticus, a prolonged seizure lasting longer than 5 minutes, according to a study sponsored by NINDS. Status epilepticus is a potentially life-threatening emergency that causes 55,000 deaths each year. Anticonvulsant drugs are typically delivered intravenously (IV) as a first-line treatment.

Starting an IV in a patient experiencing seizures can pose a challenge for paramedics and waste precious time. Giving an intramuscular shot is easier, faster and more reliable, especially in patients having convulsions. The researchers sought to determine whether an intramuscular injection, which quickly delivers anticonvulsant medicine (midazolam) into a patient's thigh muscle, is as safe and effective as giving medicine directly into a vein. The study, carried out by paramedics, compared how well delivery by each method stopped patients' seizures by the time the ambulance arrived at the emergency department. The study appeared in the Feb. 16 issue of the *New England Journal of Medicine*.

"Patients with status epilepticus can suffer severe consequences if seizures are not stopped quickly," said NINDS deputy director Dr. Walter Koroshetz. "This study establishes that rapid intramuscular injection of an anticonvulsant drug is safe and effective."

Investigators said that while autoinjectors might someday be available for use by epilepsy patients and their family members, more research is required. Because of the strong sedative effect of midazolam, on-site medical supervision is now required for the safety of the patient.

Drug Halts Organ Damage in Inflammatory Genetic Disorder

A new study shows that Kineret (anakinra), a medication approved for the treatment of rheumatoid arthritis, is effective in stopping the progression of organ damage in people with neonatal-onset multisystem inflammatory disease (NOMID). This rare and debilitating genetic disorder causes persistent inflammation and ongoing tissue damage. The research, performed by scientists at NIAMS, was published online in *Arthritis & Rheumatism*.

NOMID affects numerous organs and body systems including the skin, joints, eyes and central nervous system. The first sign of the disease is often a rash that develops within the first weeks of life. Other problems, including fever, meningitis, joint damage, vision and hearing loss and mental retardation, can follow. Kineret, one of a relatively new class of drugs known as biologic response modifiers or biologics, blocks the activity of interleukin-1 (IL-1), a protein made by cells of the immune system. IL-1 is overproduced in NOMID and a number of other diseases, leading to damaging inflammation.—compiled by Carla Garnett



Drug delivery into muscle using an autoinjector is faster and may be a more effective way to stop a seizure lasting longer than 5 minutes, according to a study sponsored by NINDS and carried out by paramedics. Above, a device used to deliver anticonvulsant medicine (midazolam) is shown with the kit paramedics carry it in.

milestones

Six NIMH Scientists Honored for Brain Research



Six National Institute of Mental Health intramural researchers were recently honored for their research on the brain and mental illness.

Dr. Leslie Ungerleider and Dr. Mortimer Mishkin each received the Grawemeyer Award for Psychology from the University of Louisville. Ungerleider, chief of the Laboratory of Brain and Cognition, and Mishkin, acting chief of the Laboratory of Neuropsychology, were cited for discovering that what is seen by the eye is routed via a different brain pathway than the one that processes where an object is located. This insight into the organization of the brain's cortex has opened the way to important advances in neuroscience.



Four NIMH intramural researchers also were among Outstanding Research Achievement Prize honorees from the Brain & Behavior Research Foundation.

Dr. Joel Kleinman, deputy chief of the Clinical Brain Disorders Branch, was among two recipients of the Leiber Prize for Schizophrenia Research. Over more than 3 decades, he has built a unique collection of post-mortem human brains that have enabled pioneering studies into the molecular roots of schizophrenia—and recently a landmark database that holds secrets

to how genetic variation affects brain structure and function.

The Ruane Prize for Child and Adolescent Psychiatric Research went to Dr. Daniel Pine, chief of the Emotion and Development Branch. Using brain imaging, genetics and other cutting-edge approaches, he is tracing the circuitry of childhood mood and anxiety disorders to their roots in the key brain centers for emotion and thinking. His research team is also developing new treatments, both pharmacological and behavioral, for children affected by these disorders.

Dr. Carlos Zarate, chief of the Experimental Therapeutics Branch, shared, with another researcher, the Bipolar Mood Disorder Prize. Zarate and colleagues are developing an experimental fast-acting antidepressant treatment strategy that lifts depression symptoms within an hour in bipolar patients. The new treatment is based on the mechanism-of-action of ketamine, a drug that works through the brain's glutamate chemical messenger system, which is thought to act closer to the seat of the problem in the brain than existing serotonin-based antidepressants.

Dr. Amanda Law of the Clinical Brain Disorders Branch was one of two recipients of the Sidney R. Baer, Jr. Prize for Schizophrenia Research. Her studies into molecular and cellular mechanisms of genetic susceptibility to schizophrenia are uncovering how variation in suspect genes leads to protein abnormalities in a pathway critical for proper brain development. The research, in adult and fetal human post-mortem brains, human and rodent cell systems and genetically engineered mice, holds promise for development of new strategies for treating developmental brain disorders.

Dr. Leslie Ungerleider (top) and Dr. Mortimer Mishkin are winners of the Grawemeyer Award for Psychology from the University of Louisville.



At left, Dr. Joel Kleinman (l), Daniel Pine (c) and Dr. Carlos Zarate are winners of the Leiber Prize for Schizophrenia Research, Ruane Prize for Child and Adolescent Psychiatric Research and Bipolar Mood Disorder Prize, respectively. At right, Dr. Amanda Law receives the Sidney R. Baer, Jr. Prize for Schizophrenia Research from Columbia University's Dr. Herbert Pardes, a former NIMH director.

NCATS Scientist Named NIH Federal Engineer of the Year

The word “engineer” comes from the Latin words *ingeniare*, meaning “to design or devise,” and the word *ingenium*, which translates to “clever invention.”

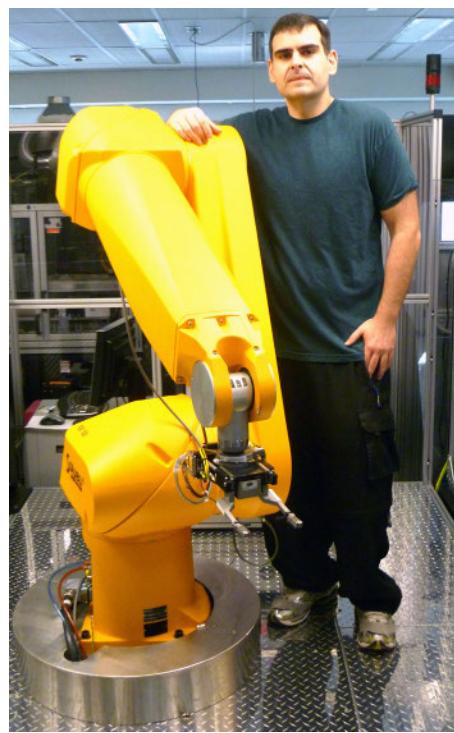
The meanings aptly describe Sam Michael of the National Center for Advancing Translational Sciences, who recently was named NIH’s Federal Engineer of the Year.

Michael received the honor at the Feb. 23 Federal Engineer of the Year awards ceremony at the National Press Club in Washington, D.C. The award, sponsored by the National Society of Professional Engineers, was in recognition of his leadership of the establishment of a world-class chemical compound screening facility at NIH.

Michael is director of automation and compound management in the Division of Pre-clinical Innovation at NCATS. He and his team create, operate,

maintain and develop improvements to a suite of automated high-throughput robotic screening systems. These systems operate on a scale equal to or greater than those at the largest pharmaceutical companies. In addition, they have made possible the development of hundreds of chemical probes that investigators worldwide use to validate new drug targets and chemical leads for development of new drugs for dozens of currently untreatable diseases.

“Hundreds of visitors have come to see and learn from our operations, and I always tell them that Sam and his team are the reason our screening technologies are world-leading,” said Dr. Christopher Austin, director of the Division of Pre-clinical Innovation and Michael’s award nominator. “It is enormously gratifying that



Sam Michael of the National Center for Advancing Translational Sciences was named NIH’s Federal Engineer of the Year.

Sam has been recognized with this honor by his engineering peers in the federal government.”

As the son of a civil and petroleum engineer growing up in Silver Spring, a young Michael started his engineering career building with Legos and making them move. Ultimately, it was this interest in making things that work that led him to a career in engineering.

“I’m excited and I appreciate being recognized for this honor. But it’s really a reflection of the incredible work of my team and the biologists, chemists and informatics scientists we work with here and the remarkable environment of this center,” said Michael.—Geoff Spencer



Research Study Volunteers Needed

Do you drink alcohol? Drink daily or almost daily? Are you between the ages of 21 and 60? NIAAA is seeking men and women to study whether a medication for smoking cessation (Chantix) may affect drinking. Volunteers should be healthy and drug-free. Qualified subjects will be reimbursed for their participation. The study lasts 9 weeks and requires 5 outpatient visits and one overnight visit at the Clinical Center. For more details, call (301) 496-7500. Refer to study 08-AA-0137.

Midlife & Menopause Research Studies Seek Healthy Volunteers

Healthy women ages 40-65 are invited to participate in outpatient research studies. Compensation is provided. Call (301) 496-9576 and refer to studies 88-M-0131 and 03-M-0175.

Did You Ever Have Postpartum Depression?

If you suffered from postpartum depression (PPD) following the birth of any of your children, consider participating in this 8-month outpatient research study at the Clinical Center. This NIMH research study is designed to examine the role of hormones in the onset of your PPD. To participate, you must be 18-50 years old with regular menstrual cycles and not taking any medications. Call (301) 496-9576 and refer to study 95-M-0097. There is no cost to participate and compensation may be provided.

'We Can't Wait'

New Steps To Fight Alzheimer's Disease

The Obama administration on Feb. 7 announced new efforts to fight Alzheimer's disease, including immediately making an additional \$50 million available for cutting-edge Alzheimer's research. In addition, the administration announced that its fiscal year 2013 budget will boost funding for Alzheimer's research by \$80 million. The announcement, made at the National Press Club in Washington, D.C., also includes an additional \$26 million in caregiver support, provider education, public awareness and improvements in data infrastructure.

"Today's announcement reflects this administration's commitment to confronting Alzheimer's, a disease that takes a devastating toll on millions of Americans," said HHS Secretary Kathleen Sebelius. "We can't wait to act; reducing the burden of Alzheimer's disease on patients and their families is an urgent national priority."

As many as 5.1 million Americans currently suffer from Alzheimer's disease, which is a progressive, irreversible brain disorder that destroys memory and thinking skills. With the aging of the U.S. population, the number of people with Alzheimer's disease could more than double by 2050.

"These projections are simply staggering," said NIH director Dr. Francis Collins. "This new funding will accelerate NIH's effort to use the power of science to develop new ways of helping people with Alzheimer's disease and those at risk."

Together, the fiscal years 2012 and 2013 investments total \$130 million in new Alzheimer's research funding over 2 years—over 25 percent more than the current annual Alzheimer's research investment.

The additional NIH research funding will support both basic and clinical research. Investments will include research to identify genes that increase the risk of Alzheimer's disease and testing therapies in individuals at the highest risk for the disease.

On the clinical side, the funds may be used to expand efforts to move new therapeutic approaches into clinical trials and to develop better databases to assess the nation's burden of cognitive impairment and dementia.



On hand at the Feb. 7 Alzheimer's announcement downtown were (from l) HHS Secretary Kathleen Sebelius, NIH director Dr. Francis Collins, HHS Assistant Secretary for Aging Kathy Greenlee and Meryl Comer, an advocate for AD research and an AD caregiver.

PHOTOS: ERNIE BRANSON

Ioannidis To Speak, Mar. 19 in Natcher

Dr. John Ioannidis, C.F. Rehnborg professor in disease prevention, professor of medicine and director of the Stanford Prevention Research Center at Stanford University School of Medicine, will speak on "The Pressure To Get It Right: Biases in Biomedical Research," on Monday, Mar. 19, from 10 a.m. to noon in Bldg. 45, balconies A, B & C.

Ioannidis will discuss empirical evidence for the presence and consequences of some main biases in scientific discovery. He will also discuss solutions for optimizing the efficiency of biomedical research processes. The intensified quest for scientific discovery has resulted in a flurry of research claims that represent false-positive or exaggerated results. There are many forces that create this excess of spurious significant findings, including both random error and a number of biases. Ioannidis' talk will address all of these issues.



Ioannidis has been adjunct faculty for Tufts University School of Medicine since 1996, with the rank of professor since 2002. Since 2008, he has been leading the Center for Genetic Epidemiology and Modeling of the Tufts Institute for Clinical Research and Health Policy Studies. He is also adjunct professor of epidemiology at Harvard School of Public Health and visiting professor of epidemiology and biostatistics at Imperial College London.

Ioannidis has served as a member of the executive board of the Human Genome Epidemiology Network, president of the Society for Research Synthesis Methodology, editorial board member of 26 international journals and editor-in-chief of the *European Journal of Clinical Investigation*. His work combines skills in clinical research methodology and evidence-based medicine with the challenges of current molecular medicine and genomics.

The seminar is sponsored by the Office of Disease Prevention and several institutes. Registration is not required; seating is on a first-come, first-served basis. Sign language interpreters will be provided. Those who require reasonable accommodation to participate should contact Paris Watson at Paris.Watson@nih.gov or (301) 496-6615.