FEBRUARY 14, 2014
VOL. LXVI, NO. 4
The Second Best Thing About Payday

nih record

ABOVE • *Cattle markets in Mali allow researchers to learn how ticks act as vectors of disease. See story on p. 5.*

features

departments

'Why Are We Here?'

Casadevall Speaks on Origins of Microbial Virulence

By Belle Waring

What killed the dinosaurs? In his recent Joseph J. Kinyoun Memorial Lecture, Dr. Arturo Casadevall offered the possibility that the fall of the reptiles and rise of mammals were linked by differing susceptibility to fungal diseases.

Professor and chair of the department of microbiology and immunology at Albert Einstein College of Medicine of Yeshiva University in New York, Casadevall argued that science can be fun.

"In biology, we don't think any more," he said. "In fact, we can't think without data, and I think that's one of the things that we have lost."

Dr. Arturo Casadevall gives Kinyoun Lecture.

His talk embodied fearless scientific thought in action. He explained how Darwin wouldn't get published today, confronted the current state of scientific publication, posed fundamental questions usually not heard in scientific talks and redefined virulence.

SEE **CASADEVALL**, PAGE 6

Reconnect to the 'Why'

Former Navy SEAL Greitens Offers a New Meaning of 'Frontline'

By Dever Powell

When Dr. Eric Greitens, former Rhodes scholar turned Navy SEAL, says "frontline," it's hard not to imagine a battlefield in Iraq or Afghanistan.

A military frontline is well understood by servicemen and women: it's a place of pain, hardship and fear, a place where victories are won and friendships are formed.

Dr. Eric Greitens, former SEAL, speaks at NIH.

But a frontline is not just a military term.

"Every person has a frontline," Greitens said recently in Masur Auditorium, where

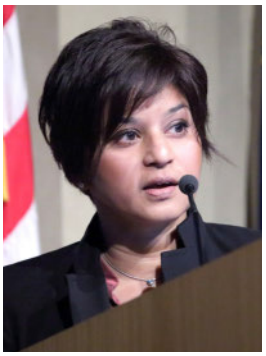
SEE **GREITENS**, PAGE 4

Get Moving

Exercise Your Way to a Longer, Healthier Life, Forum Speakers Urge

By Dana Steinberg

If people were aware of the litany of health benefits that arise from regular exercise, even the busiest among us would make it a priority. Keeping fit confers major health benefits—that message resonated at a recent Staff Training in Extramural Programs (STEP) forum, "Move: Physical Activity Benefits Everyone," held in NLM's Lister Hill Auditorium.



NIA's Dr. Chhanda Dutta

Research shows that regular exercise helps lower the risk of early death, heart disease, stroke, high blood pressure and type 2 diabetes. In seniors, increased physical activity can

SEE **EXERCISE**, PAGE 8

The **NIH Record** is published biweekly at Bethesda, MD by the Editorial Operations Branch, Office of Communications and Public Liaison, for the information of employees of the National Institutes of Health, Department of Health and Human Services. The content is reprintable without permission. Pictures may be available upon request. Use of funds for printing this periodical has been approved by the director of the Office of Management and Budget through September 30, 2014.

To receive alerts to our latest issue, send an email to listserv@list.nih.gov with the words "Subscribe NIHRECORD" in the message body.

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

Associate Editor
Carla Garnett
Carla.Garnett@nih.gov

Staff Writers
Jan Ehrman
Jan.Ehrman@nih.gov

Dana Steinberg
Dana.Steinberg@nih.gov

Belle Waring
Belle.Waring@nih.gov

The **NIH Record** reserves the right to make corrections, changes or deletions in submitted copy in conformity with the policies of the paper and HHS.

NIH...Turning Discovery Into Health

nih record

briefs

NIH Rare Disease Day, Feb. 28

NIH celebrates the seventh annual Rare Disease Day on Friday, Feb. 28 from 8:30 a.m. to 5 p.m. Patients, visitors and staff are welcome to attend presentations and participate in activities in the Clinical Center's Masur Auditorium, offered by the NCATS Office of Rare Diseases Research and the Clinical Center. Attendance is free and open to the public. In association with the Global Genes Project, all attendees are encouraged to wear their favorite pair of jeans. For more information, including details on registration and an agenda, visit http://rarediseases.info.nih.gov/RareDiseaseDay.aspx.

NIH Management Intern Program Recruits

Unlock a new career path with the NIH Management Intern Program, which is recruiting Apr. 7-11. The MI Program is a highly competitive, 2-year career-development program for current NIH employees. MIs come from a variety of job backgrounds including both scientific and administrative fields. Upon completion of the program, MIs transition into an administrative-management career in one of many areas throughout the NIH enterprise. Eligible employees are invited to apply. For program FAQs, upcoming information sessions and details about eligibility, visit http://trainingcenter.nih.gov/intern/mi/.

Sailing Association Open House, Feb. 27

The NIH Sailing Association invites everyone to its open house on Thursday, Feb. 27 from 5 to 8 p.m. at the FAES House at the corner of Old Georgetown Rd. and Cedar Ln. Explore your interest in learning to sail and discover opportunities for sailing with NIHSA. There will be information about 6-week basic training classes, the club's racing program and social activities offered by NIHSA. A fee of $5 at the door includes pizza, drinks and snacks. Cash bar for beer and wine—$2 each. Look for NIHSA posters and flyers around campus. For more information, visit www.recgov.org/sail.

Sign Up for *NIH Record* Reminders

Did you know that, with the click of a button, you can sign up for email reminders when a new *NIH Record* hits the streets?

"The Second Best Thing About Payday" has been informing NIH'ers since 1949. Whether you prefer the paper or electronic version, make sure you don't miss anything. Visit http://nihrecord.od.nih.gov/ for two easy options to subscribe.

For 65 years, the *NIH Record* has helped create a sense of unity and community at NIH, reflecting the breadth of a great institution from its science and policies to its people and facilities. At the link above, you can find every issue online in our archives.

Sign up today to get your *NIH Record*. After all, you may be in it.

Next Protocol Navigation Lecture, Mar. 3

The IRP Protocol Navigation Training Program Seminar Series continues with a lecture on Monday, Mar. 3 from 2:30 to 3:30 p.m. in Lipsett Amphitheater, Bldg. 10. The program is a trans-NIH effort to develop resources and tools and to provide training for intramural staff and contractors involved in protocol development, writing, coordination and management. Jennifer Morris, NINDS PTMS liaison, will present, "NIH Protocol Tracking and Management System (PTMS): What's New and What's Next for 2014?" For more information, contact Beverly Barham, (301) 594-2494, bbarham@mail.nih.gov or Marcia Vital, (301) 451-9437, vitalm@mail.nih.gov.

Cold Enough for You?

Been a heckuva winter, eh? While it has been shown scientifically that occasional polar vortices build character, they do nothing for bicycles. This poor specimen took the brunt of winter tied to a fence near Metro/Gateway. But take heart—Bike to Work Day is only 3 months away. Anyone want to bet when the first daffodil will raise its scarved head in front of Bldg. 31?

PHOTO: BILL BRANSON

New PI Dashboard Launches, Feb. 18

The Division of Occupational Health and Safety announces the rollout of its new PI Dashboard electronic registration system (Nexus) for pathogen and rDNA work applications. The system goes live on Feb. 18 and will be accessible online at https://oms.ors.nih.gov/. For details, contact your institute/center-assigned safety specialist or NIH biological safety officer Dr. Richard Baumann, baumannrg@mail.nih.gov. For more safety information, visit www.ors.od.nih.gov/sr/dohs/aboutDOHS/Pages/about_dohs.aspx.

Maddox Launches Diversity Seminar Series at CSR

By Don Luckett

"Diversity is the only true thing we all have in common, so we should celebrate it," said Dr. Yvonne Maddox, NICHD deputy director, who recently helped launch a staff seminar series sponsored by CSR's new diversity committee.

"Yvonne is one of the spectacular success stories of NIH," said Dr. Richard Nakamura, CSR director. "Her career and way of making progress are a great inspiration."

Maddox titled her talk "Since Arriving: NIH Then and Now" and shared lessons she learned rising up the ranks at NIH.

In 1985, she joined NIGMS as a health scientist administrator. It wasn't long before she was named chief of the institute's physiology sciences section.

While at NIGMS, Dr. Ruth Kirschstein, former NIH deputy director, encouraged Maddox to apply to be NICHD's deputy director. It was a big jump and Maddox had her doubts. "Even if you don't get the job," said Kirschstein,"you'll have made a positive impression that you're someone to look out for."

In early 1995, Maddox got the job and came to enjoy it. In 2000, Kirschstein again encouraged her forward—asking her to become acting NIH deputy director.

Today, Maddox is well known for being a mentor to many. She encourages others to reach out to people who can guide and coach them. "Don't just look for folks who look like you," she said. "Get help from anybody you think can take you a step further in your career. Listen to advice and never be afraid to take chances. You may not always succeed, but if you don't try, you will never get ahead."

Maddox said one of the keys to having a successful career is to have a grounded and positive approach to work. "Who am I and how can I contribute?" are the questions every employee should ask. Maddox listed the pillars of her approach to success:

- Work from your strengths and set high expectations.
- Keep a sense of optimism.
- Make your own luck and find your own way to your dreams.
- Have an exceptional work ethic.
- Always see yourself as a role model.

Setting high expectations and pursuing them is not just a philosophy; it's a way of life for Maddox. She has led major scientific advances related to women's and children's health, health disparities and underserved populations in America. She counts herself blessed for the way NIH embraced her from day one.

Maddox said much still needs to be done to increase diversity at NIH and in the extramural community. After mentioning some of NIH's key diversity programs, she focused on what individuals can do:

- Value diversity. This value will reverberate to others.
- Embrace the diversity of your colleagues and together you will make each other better at what you do.
- Know that you can make a difference and use your abilities to do it.

She is heartened by the increased attention NIH is giving to advancing diversity. "I have seen what NIH can do when it sets its mind to it," she said. "I am hopeful."

APAO Presents Annual Awards

The NIH Asian and Pacific Islander American Organization (APAO) held its annual awards ceremony recently. Sharon Wong (l), deputy director for coordination & policy in the Office of Personnel Management's Office of Diversity & Inclusion, presented opening remarks at the ceremony. Honorees (starting second from l) include Dr. Wei Yang of NIDDK (for scientific achievement), Dr. Abraham Bautista of NIAAA (for leadership excellence) and JoAnne Wong of NCATS (Kuan-Teh Jeang Distinguished Service Award). Dr. Richard K. Nakamura (third from r), director of the Center for Scientific Review, presented the keynote address. Dr. Xinzhi Zhang (r), APAO president, and Dr. Shioko Kimura (second from r), chair of the APAO awards committee, presented the awards.

PHOTO: RUBY LEE

GREITENS

CONTINUED FROM PAGE 1

***Above**:*
Greitens uses Navy SEAL training to motivate NIH leadership.

PHOTOS: ERNIE BRANSON

This is a call to arms for every public servant: It's not about you, your ego, your career; it's about the people you serve.

he gave a talk in the Deputy Director for Management Seminar Series. A dynamic lecturer and role model, he spoke on "Inspired Leadership in Challenging Times," launching this year's DDM series in robust fashion.

"We all have a place where we are challenged," Greitens said. "That place is your frontline."

Greitens offered ways to enhance service to others, overcome obstacles and successfully navigate new frontlines. He engaged the audience by showing examples from Navy SEAL (sea, air, land) training and his current work reconnecting veterans with new life purposes.

"People can be overwhelmed by the 'how' of any new situation or new challenge," he said.

Sometimes the answers are right in front of you: the people whom you serve.

Greitens demonstrated his point by showing videos of SEAL training, including "drown-proofing," an extreme underwater challenge, and segments of "Hell Week." How do trainees successfully meet such relentless tests and make it through?

Greitens said the strongest in the class were not necessarily the incoming stars but those who stepped out of their self-concern and focused on other people.

For example, one test of endurance required one person to carry another during the final leg of a long course. Greitens said the key to meeting this challenge, enduring the pain and taking one more step was focusing on the person you are carrying.

"You've got to remember this," Greitens said. "There's someone counting on you and you can be strong for them."

This is a call to arms for every public servant: It's not about you, your ego, your career; it's about the people you serve.

Greitens said people quit the training when they convinced themselves they couldn't endure one more step.

"You must be willing to do the hard things, to make hard decisions about growth."

Every time you decide to move one more step through pain, your character evolves. The SEAL instructors call these voluntary decisions "evolutions."

"Do the hard thing in front of you again and again," Greitens said, "and eventually you change who you are and how you can be of service."

Greitens used his combat pay from Iraq to co-found Mission Continues, an organization that empowers returning veterans to continue to serve on new frontlines and is a model for public service and an inspiration for changing your life.

"Everyone can serve," Greitens said. "Everyone has something to offer."

One challenge for a returning veteran facing a new frontline can be discovering what the next chapter is going to look like.

Greitens said it's all about bringing clarity to the "why": "If you have the right why, you can make it through anything."

He urged NIH'ers to reconnect with the "why."

For example, if the "why" gets lost when teams collaborate on projects or when supervisors communicate with employees, Greitens said, it's difficult to make progress. In fact, without the "why," can there be progress at all? It's all about serving others.

"Push yourself and challenge yourself," Greitens said. "We need all of that on the frontlines, when we build teams, when we make a difference."

Archived webcasts of the DDM Seminar Series are available at http://videocast.nih.gov/PastEvents.asp?c=147.

NIAID Research Thrives in Mali

By Ken Pekoc

NIAID scientists and their colleagues have expanded the focus of collaborative studies at the International Center for Excellence in Research (ICER) in Mali to include several diseases recently identified in the West African nation: tick-borne relapsing fever (TBRF), Lassa fever and Crimean-Congo hemorrhagic fever (CCHF).

The NIAID Division of Intramural Research has conducted studies in Mali since 1990. The ICER, established by NIAID in 2002, is part of the medical school campus at the University of Sciences, Techniques and Technologies of Bamako in Mali's capital. Its original goal was to serve as a focal point for malaria research, engaging Malian and NIAID scientists in studies involving mosquitoes, malaria drug resistance and candidate malaria vaccines. Subsequent cooperation included research on neglected tropical diseases such as filariasis and leishmaniasis as well as studies of individuals co-infected with HIV and tuberculosis.

The scope of the collaboration expanded again in 2008 and 2010 when scientists from NIAID's Rocky Mountain Laboratories (RML) identified the TBRF bacterium and Lassa fever virus in rodents obtained from Mali villages. More recently, the same visiting scientists identified CCHF virus in Malian ticks.

TBRF is rarely fatal and can be treated with antibiotics. However, there is no vaccine or widely accepted treatment for Lassa or CCHF. Each year, an estimated 100,000 to 300,000 people in West Africa are infected with Lassa, leading to approximately 5,000 deaths. Case reports for CCHF are not available, though the mortality rate ranges between 10 and 40 percent, according to the World Health Organization. CCHF occurs in Africa, the Balkans, the Middle East and Asia.

NIAID's CCHF project in Mali also has expanded research partnerships to include veterinarians and ranchers. Together they hope to more efficiently identify regions where the disease may be widespread in cattle.

CCHF is typically transmitted to humans either by a tick bite or through contact with infected tissue or fluids from cattle. The researchers already have identified some regions of high incidence for TBRF and Lassa and are hoping soon to receive permission to obtain human blood samples to assess infection prevalence.

Weekly cattle markets in Mali provide NIAID researchers with access to ticks that serve as vectors for diseases such as Crimean-Congo hemorrhagic fever virus.

Through this collaboration, NIAID scientists also are sharing expertise and resources with Malian clinicians so that they can detect disease-causing organisms in their patients.

The NIAID projects also have helped U.S. and Malian scientists collect nearly 4,000 ticks in Mali. These ticks, collected at cattle markets, are being analyzed at RML for multiple infectious agents. RML also plans to use the ticks to establish a colony for use in future studies of CCHF transmission. The group also seeks to obtain rodents from Mali to establish a Lassa fever study model.

Dr. Dave Safronetz is leading the Lassa and CCHF projects for NIAID's Laboratory of Virology. Dr. Tom Schwan is leading the TBRF project for the Laboratory of Zoonotic Pathogens. Both say that the studies have been scientifically rewarding and highly productive.

Members of different lab organizations—bacteriologists and virologists—are studying the same specimens while also teaching Malian physicians about new infectious diseases. Because the symptoms of these diseases often mimic malaria, these researchers also are focusing on training that will allow local physicians to more accurately diagnose a range of infectious diseases so they can be treated effectively.

DeGregory To Present Brown Bag On Civil Rights

NIH's 2014 African American History Month Brown Bag Lunch and Learn is set for Thursday, Feb. 27 from 11:30 a.m. to 12:30 p.m. in Wilson Hall, Bldg. 1. The featured presenter is Dr. Crystal A. deGregory, founder and executive editor of HBCUSTORY.com, an online advocacy center that offers inspiring stories of the Historically Black Colleges and Universities (HBCU) community. She will discuss "Herstory: Civil Rights (and Wrongs) at Home and Abroad." For program details, contact Victoria A. Gross at grossv@mail.nih.gov or (301) 451-0746.

CASADEVALL

CONTINUED FROM PAGE 1

***Above**: Casadevall investigates* Cryptococcus neoformans, *a common fungus that is harmless to healthy people but can cause serious disease in immune-compromised people.*

PHOTOS: BILL BRANSON

With the fungus *Cryptococcus neoformans* as a model, Casadevall sees virulence (disease severity) as a framework in which damage can come from the host, microbe or both.

This idea frees you, he says, from approaches that have created "a microbiological archipelago" with specialties that barely interact with each other.

Casadevall, like Darwin, is looking for patterns.

In 1899, fungal diseases were rare; by 1999, they had become "distressingly common." Why?

"We changed the host," he said. Medical progress made us more vulnerable to fungi. And then came "the cataclysm of AIDS."

A common fungus usually harmless to healthy people, *C. neoformans* can cause serious illness in immune-compromised people such as those with HIV/AIDS.

"*C. neoformans* is one of the leading causes of death in Africa, eclipsing tuberculosis, and yet you don't hear about it," Casadevall said.

Fungi, with over 1.5 million species, are major pathogens of plants, reptiles, invertebrates and amphibians and are now devastating ecosystems of bats (which are mammals) and frogs.

Still, there are very few fungi harmful to mammals with intact immunity. Could the answer be in the distant past?

The age of mammals begins after the K-T event, a mass extinction of three-quarters of plant and animal species on Earth—including all non-avian dinosaurs.

Most scientists believe that K-T was triggered by a massive comet/asteroid impact. Fires, smoke and dust obscured the sun and photosynthesis was arrested for over 6 months.

Yet the mass extinction gave mammals a chance to produce new forms, such as whales and primates.

"But if reptiles were so fit, why did they not reclaim the Earth?" Casadevall said. The larger ones were likely killed by the impact of the blast, the disruption of food sources, the chilling of the planet and fungal diseases. However, some reptiles survived. Given the advantages of reptiles over mammals on energy consumption, one wonders why the cataclysm was not followed by a recovery of reptiles and a second reptilian era.

Imagine a primeval forested planet where all trees have fallen, creating a massive compost layer for fungi to feast on.

The animals that made it were largely warm-blooded. Although dinosaurs were warm-blooded, they could not have regulated their temperatures the way we do.

This is key: Most fungal species do not threaten mammals because fungi do not tolerate the mammalian core temperature range. We are too warm for them.

Thus fungal selection acted as a filter for the emergence of mammals, he argued.

"I have no proof, no experiment. It's all thought…I have no idea if it's accepted and I frankly don't care. I never have to apply for funding for this and this is fun, this is why I went into science.

"We should be able to write and debate things," he said, "and this is something you don't see too much any more."

Meanwhile, his work on *Cryptococcus neoformans* is backed up by 20 years of research and publication. Collaborating with physicists, chemists and geneticists, Casadevall developed new insights.

A fungus that lives in the soil, *C. neoformans* probably developed its virulence through interactions with amoebae over the last billion years. Using both microscopic and quantum models, he found that the *C. neoformans* capsule appears to be a dendrimer, a repetitively branched molecule that is "incredibly unusual. This raises huge basic science questions…that are very biologically relevant." This work is ongoing.

Turning to melanins, pigments found in all animal kingdoms, Casadevall reviewed their protective function as "nonspecific armor."

He found that melanin in fungi shows that they use radiation for food.

"We thought we had a major discovery," he said, but two "single-word journals" rejected it.

Nonetheless, the news sections of those same journals, and many others, covered these findings.

"We should be able to write and debate things," Casadevall said, "and this is something you don't see too much any more."

Tracing his paper's progress, Casadevall addressed the state of scientific publication today. His follow-up study showed that "misconduct accounts for the majority of retracted scientific publications" and that "males are responsible for a lot of this."

This got a laugh from the audience, but Casadevall cautioned that "all we show is that the females are missing," raising the possibility that males and females carry out misconduct at the same frequency, but that females don't get caught.

With his fungi and radiation study now confirmed by another journal, Casadevall insists that fungi do have a limited ability to photosynthesize (convert energy from the sun and other sources of radiation), turning blue-green and black in the process.

And the *in vivo* application? Ingestion of melanin in black mushrooms (an edible fungus) can protect mice against lethal irradiation.

"We hope to go into clinical trials. It has tremendous potential usefulness in radiation therapy."

Meanwhile, as the climate warms, many nonpathogenic fungi may adapt to higher temperatures enough "to take down immunologically intact humans."

He does not have a predictive model and can find "no chaotic signatures" in his own model for virulence. (Chaos means that small differences translate into big changes.) Nonetheless he keeps asking fundamental questions.

"Think about it," he said. "We don't know why we can make vaccines very easily for some organisms and not others. Wouldn't you want to know if the system you're working with is chaotic or not? Yet something so fundamental has never been asked. Are our immune responses chaotic?"

And the answers to his existential questions from a fungal point of view?

- Why are we here? *K-T event and fungal selection*.
- Why are we so hot? *To keep the fungi away*.
- Why do we eat so much? *To maintain high temperature*.
- Why are mammals the dominant large animals? *Fungal selection kept down the reptiles. No second age of reptiles!*

"Mammals make no sense without the fungi," he says. "Mammals were going nowhere until the K-T event."

If you bring infected frogs into a 37-degree room (normal human temperature at Celsius) it will completely eradicate the fungus. Perhaps, he said, global warming will save the frogs by roasting the fungus.

"And I leave you with that image," he concluded. "That perhaps somebody will benefit from all that pollution."

The talk is archived at http://videocast.nih.gov/summary.asp?Live=13248&bhcp=1.

NIH Holds Diversity Workshop, Taps Experts

Recently, NIBIB director Dr. Roderic Pettigrew, who is also acting chief officer for scientific workforce diversity, with support from NIH director Dr. Francis Collins and NIH principal deputy director Dr. Lawrence Tabak, held a "Diversity at NIH" workshop.

Prominent researchers from across the country came to NIH to present a case for diversity. Experts educated NIH leadership and the community about the psychosocial and psychological phenomena that influence perceptions and social interactions, which may interfere with enhancing diversity.

Dr. Brian Nosek of the University of Virginia demonstrated how an unwanted bias is a consequence of ordinary cognitive processes, which helps explain why it can be difficult to change a perception even when we become aware of it. Stanford University's Dr. Hannah Valantine, who was recently appointed by Collins to be NIH's first permanent diversity officer (see story on p. 10), shared results that identified physiological manifestations of stereotype threat and how those "triggers" can be used to develop interventions. Dr. Pauline Rose Clance of Georgia State University, the first to characterize the "impostor phenomenon," shared how common it is to feel like you are not good enough at work; for some, those feelings can be extreme and threaten their success.

The workshop challenged the audience to consider ways to bring changes to policies and programs that will enhance diversity. Dr. Marc Nivet of the Association of American Medical Colleges asked NIH to bring rigor to solve the complex issues of diversity and inclusion, much as it does to solve complex scientific problems. And as UNC's Dr. Joseph DeSimone stated, we often learn the most from those with whom we have the least in common. Diversity, he said, is a fundamental tenet for innovation.

To encourage dialogue about diversity post-workshop, Rice University's Dr. Erin Cech stressed the need to talk about these issues regularly, outside of workshops and meetings. Dr. Jack Dovidio of Yale stressed how we need to be color conscious and attentive to the inequalities that exist because colorblindness and common identity do not translate into social action and only reinforce the status quo.

As for next steps, Collins asked the IC directors to continue the discussion with their staff and identify barriers preventing diversity. In order to achieve a diverse and inclusive workforce at NIH, diversity needs to become a priority, policies and programs need to be in place to overcome psychological and social obstacles and interventions need to be effective and long-lasting.

The workshop is archived at http://videocast.nih.gov/summary.asp?Live=13316.—**Irene Avila**

EXERCISE

CONTINUED FROM PAGE 1

***Above**:*
The STEP panel included (from l) Dr. Jerry Phelps, Dr. Greg Cartee, Dutta and Dr. Russell Pate.

***Below**:*
Pate has finished in the top 10 at the Boston Marathon, but concedes that exercise need not be intensive to provide benefit.

PHOTOS: ERNIE BRANSON

improve bone density, balance, sleep quality and may improve cognitive function."

The American College of Sports Medicine (ACSM) first established clinical guidelines on exercise in 1975. The recommendation was to exercise at 70-90 percent capacity 3- 5 days per week. By 1991, while the frequency remained the same, the ACSM modified the intensity level to a range of 40-85 percent.

"There was a growing awareness among the scientific community as well as the clinical community that the intensity of exercise probably didn't have to be as great as initially thought in order to provide important health benefits," said Dr. Russell Pate, professor in the department of exercise science in the Arnold School of Public Health, University of South Carolina.

The HHS Physical Activity Guidelines recommend adults get 2½ hours per week of moderate intensity aerobics or half that amount in vigorous activity. In addition, it is recommended that adults do muscle-strengthening activities at least 2 days per week.

Physical activity has an impact on many tissues and organs, said Dr. Greg Cartee, associate dean for research at the school of kinesiology, University of Michigan. He defined physical activity as "any movement produced by the contraction of skeletal muscle that increases energy expenditure above basal levels."

Effects that occur during, or just after, a single exercise session are acute responses, such as increased heart rate or some longer-lasting effects such as increased muscle glucose uptake, said Cartee, who is also director of the Muscle Biology Laboratory at Michigan. Many more changes occur at the cellular level, as various enzymes and proteins work to regulate metabolism and the effects of exercise.

The effects of exercise are cumulative, said Cartee. Chronic adaptations are the continuing effects of regular, repeated bouts of acute exercise. But the positive outcomes will reverse in time if people don't remain regularly physically active.

"Many of [the benefits] are lost in a matter of days or weeks," he said. These positive adaptations over time will increase endurance, with the extent of the benefits being related to the "exercise dose," which is determined by the duration, frequency and intensity of the workout.

Dr. Jerry Phelps, a program analyst with NIEHS, knows a thing or two about endurance. Once an avid runner, he suffered an injury that inspired him to get a bicycle in 2003. He became a devoted cyclist. Phelps began by joining a *randonneurs* club, a group of noncompetitive, long-distance cyclists.

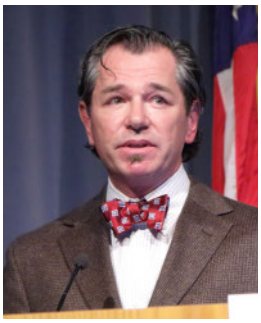
"I set some intermediate goals," he recounted. "And I did my first single-day 100-mile ride in 2003." He has twice completed the 750-mile Paris-Brest-Paris, the oldest continuously offered bike ride in the world. To build up to this event, he completed smaller qualifying rides, 100-400 miles each. Over the last decade, he has participated in more than 200 different bike events and cycled more than 50,000 miles.

While not everyone exercises at that intensity, Pate, who has twice placed in the top 10 of Boston Marathon finishers, and Phelps both started with modest goals. Even if you've let your exercise routine lapse for some time, it's never too late to begin again. "Having been fit at one point, and staying fit, substantially reduces your risk of mortality," said Dr. Chhanda Dutta, chief of the Clinical Gerontology Branch, NIA.

Regular physical activity is equally important for older adults, many of whom suffer symptoms of chronic disease and might not know where to start. In 2012, NIA launched Go4Life, a national fitness campaign to help older adults incorporate exercise into their daily lives, including motivational tips for the more sedentary folks. The campaign recommends older adults exercise a minimum of 300 minutes per week, to develop strength, balance, flexibility and endurance.

Another concern with the aging population is sarcopenia, the loss of muscle mass. Dutta said data shows sarcopenia can begin in people as young as their mid-40s; the decrease in muscle mass only progresses from there.

"No one is ever too old to exercise," said Dutta, "and you can always reap some kind of benefit by engaging in exercise."



Phelps (l) biked his way to fitness and Cartee warned that letting up on exercise means letting up on the benefits of fitness.

digest

Risks of distracted driving were greatest for newly licensed teen drivers, who were substantially more likely than adults to be involved in a crash or near miss while texting or engaging in tasks secondary to driving, according to researchers.

Study Shows Crash Risks Greatest for Teens

Drivers eat, reach for the phone, text or otherwise take their eyes off the road about 10 percent of the time they are behind the wheel, according to a study using video technology and in-vehicle sensors. The study of drivers in the Washington, D.C., area and in southwestern Virginia appeared in the Jan. 2 *New England Journal of Medicine*.

Risks of distracted driving were greatest for newly licensed teen drivers, who were substantially more likely than adults to be involved in a crash or near miss while texting or engaging in tasks secondary to driving, according to the researchers from NIH and Virginia Tech.

"Anything that takes a driver's eyes off the road can be dangerous," said study co-author Dr. Bruce Simons-Morton of NICHD, where the study was conducted. "But our study shows these distracting practices are especially risky for novice drivers, who haven't developed sound safety judgment behind the wheel."

Study Launched on Use of Genetic Sequencing To Improve Patient Outcomes

A pilot trial to assess whether assigning treatment based on specific gene mutations can provide benefit to patients with metastatic solid tumors was launched recently by NCI. The Molecular Profiling-based Assignment of Cancer Therapeutics, or M-PACT, trial is one of the first to use a randomized trial design to assess if assigning treatment based on genetic screening can improve the rate and duration of response in patients with advanced solid tumors. A trial in which patients are randomly assigned to various treatment options is the gold-standard method for determining which treatment option is best.

"Patients will have their tumors genetically screened and if a pre-defined mutation is found, they will receive treatment with targeted agents," said principal investigator Dr. Shivaani Kummar. "What we don't know, however, is whether using this approach to assign targeted treatments is really effective at providing clinical benefit to patients, as most tumors have multiple mutations and it's not always clear which mutation to target and which agent is most likely to provide maximal benefit. This study hopes to address some of these questions in the context of a prospective, randomized trial."

Bladder Cancer Study Reveals Potential Drug Targets

Investigators with The Cancer Genome Atlas (TCGA) Research Network have identified new potential therapeutic targets for a major form of bladder cancer, including important genes and pathways that are disrupted in the disease. They also discovered that, at the molecular level, some subtypes of bladder cancer—also known as urothelial carcinoma—resemble subtypes of breast, head and neck and lung cancers, suggesting similar routes of development.

The researchers' findings provide important insights into the mechanisms underlying bladder cancer, which is estimated to cause more than 15,000 deaths in the United States in 2014. TCGA is a collaboration jointly supported and managed by NCI and NHGRI.

"TCGA Research Network scientists continue to unravel the genomic intricacies of many common and often intractable cancers," said NIH director Dr. Francis Collins. "These findings are defining new research directions and accelerating the development of new cancer therapies."

In this study, published online Jan. 29 in *Nature*, investigators examined bladder cancer that invades the muscle of the bladder, the deadliest form of the disease. The current standard treatments for muscle-invasive bladder cancer include surgery and radiation combined with chemotherapy. There are no recognized second-line therapies—second choices for treatments when the initial therapy does not work—and no approved targeted agents for this type of bladder cancer. Approximately 72,000 new cases of bladder cancer will be diagnosed in the U.S. in 2014.

"This project has dramatically improved our understanding of the molecular basis of bladder cancers and their relationship to other cancer types," said lead author Dr. John Weinstein of the University of Texas MD Anderson Cancer Center. "In the long run, the potential molecular targets identified may help us to personalize therapy based on the characteristics of each patient's tumor."

"The real excitement about this project is that we now have a menu of treatment and research directions to pursue," said a senior author of the paper, Dr. Seth Lerner of Baylor College of Medicine. "The field is poised to use this information to make new advances toward therapies for a very-difficult-to-treat form of bladder cancer."—**compiled by Carla Garnett**

milestones

Stanford's Dr. Hannah Valantine will become NIH's first chief officer for scientific workforce diversity this spring.

Valantine Named 1st Chief Officer for Scientific Workforce Diversity

Dr. Hannah Valantine is NIH's first chief officer for scientific workforce diversity. NIH director Dr. Francis Collins announced the appointment Jan. 30, following a nationwide search. Valantine will lead NIH's effort to diversify the biomedical research workforce by developing a vision and comprehensive strategy to expand recruitment and retention and promote inclusiveness and equity throughout the biomedical research enterprise.

Currently serving as senior associate dean for diversity and leadership at Stanford School of Medicine, she's expected to begin her NIH role this spring.

"Recruiting and retaining the brightest minds regardless of race, ethnicity, gender, disability and socioeconomic status is critically important not only to NIH, but also to the entire U.S. scientific enterprise," said Collins. "Hannah possesses the experience, dedication and tenacity needed to move NIH forward on this critically important issue."

The newly created position dedicated entirely to diversity stems from a recommendation by the biomedical research workforce diversity working group of the advisory committee to the NIH director. Valantine will work closely with the institutes and centers, NIH grantee community and other stakeholders to ensure engagement on the issue at all levels.

At Stanford, Valantine has also served as professor of cardiovascular medicine at the university's medical center. She studied biochemistry at London University and attended St. George's Hospital Medical School. She completed postgraduate work in cardiology at two London hospitals, Brompton and Hammersmith. She moved to the U.S. to train as a fellow with leading cardiologists and cardiac surgeons, including heart transplant pioneer Dr. Norman Shumway.

In addition to a career in cardiology, Valantine is a past recipient of the NIH Director's Pathfinder Award for Diversity in the Scientific Workforce and has a proven record on implementing diversity initiatives in academic medicine.

In announcing the selection, Collins also thanked NIBIB director Dr. Roderic Pettigrew, who served as the acting chief officer for scientific workforce diversity while the search to fill the role permanently was under way.

"Roderic did an incredible job of keeping the initiative moving while continuing to serve as director of the National Institute on Biomedical Imaging and Bioengineering," Collins noted. "His tireless efforts and knowledge on this important topic will make him an essential resource to Hannah."

NIDA's Huestis Chosen for New Forensic Science Commission

Dr. Marilyn Huestis, chief of the chemistry and drug metabolism section in NIDA's Intramural Research Program, has been selected as an *ex officio* member of the newly created National Commission on Forensic Science.

Cochaired by the Department of Justice and Department of Commerce, the commission includes experts and researchers in forensic science as well as judges, attorneys and law enforcement officials. The commission will help improve the practice of forensic science and develop policy recommendations for the U.S. attorney general.

Huestis is a past president of the Society of Forensic Toxicologists, past chair of the toxicology section of the American Academy of Forensic Sciences and the first woman president of the International Association of Forensic Toxicologists.

At NIDA, she researches ways to minimize the public health impact of drugged driving; effects of marijuana or cannabinoids in the body as well as how the body absorbs, distributes, metabolizes and excretes these substances; the impact of drugs on the developing fetus; and identification of designer drug metabolites that currently elude typical drug-testing procedures.

CC Senior Advisor Gallelli Retires

On Jan. 3, Dr. Joseph Gallelli retired as senior advisor for biotechnology product development in the Clinical Center's Office of the Director. In this role, he supported development of the cell processing section in the transfusion medicine department; it manufactures cellular therapy products for treatment of CC patients.

Gallelli began his NIH career in 1961 as a staff pharmacist after completing graduate studies at Temple University, where he earned a master's and Ph.D. Soon after, he became chief of the pharmaceutical development section. By 1970, he became chief of the pharmacy department. In 1995, after completing a long and distinguished career in pharmacy, Gallelli was named senior advisor for biotechnology product development.

Gallelli has been a leader in helping transform pharmacy into a clinical profession with a focus on patient care and improving drug therapy outcomes. "[He] led an impressive and important career in decades of work for the NIH and the department," said HHS Secretary Kathleen Sebelius when she honored Gallelli for 50 years of federal service in 2011.

In 1974, Gallelli published the first textbook on the compatibility and chemical stability of drugs used in the preparation of intravenous additive solutions. The book, *Parenteral Drug Information Guide*, was based on years of research in his lab. That same year, he established the first postgraduate hospital pharmacy residency program at the Clinical Center and has mentored numerous pharmacists and scientists who have become leaders in their own right.

He also published major guidelines and recommendations on the safe handling, chemical inactivation and disposal of injectable antineoplastic drugs. Gallelli introduced the Unit Dose Drug Distribution System, which has become the standard in the U.S., and developed the first centralized intravenous admixture service for preparing sterile injectable products.

In 1982, he established the Clinical Pharmacokinetics Research Laboratory to analyze drug concentrations in biological specimens, determine the pharmacokinetic properties of investigational drugs and perform therapeutic drug monitoring to assist in individualized dosing of medications.

Gallelli has held leadership positions in numerous organizations in the U.S. and abroad, including the American Society of Health-System Pharmacists, U.S. Pharmacopeia and International Pharmaceutical Federation.

He has received awards such as the Public Health Service George Archambault Public Health Service Career Achievement Award in Pharmacy, the American Public Health Association Distinguished Federal Pharmacist Award and the Association of Military Surgeons of the U.S. Andrew Craigie Award.

In retirement, Gallelli will write about the history of pharmacy at NIH, take Italian language lessons, paint Byzantine-style icons and travel. He will not be too far away from NIH though; he has signed on to work as a special volunteer.

Members of the Hernandez family and members of the Milton Hernandez legacy working group met recently. They include (from l) Ann London; Tamara Lewis-Johnson; Matthew Fenton, director, Division of Extramural Affairs, NIAID; Andrea Hernandez; Lidia Hernandez; Diego Hernandez; Paula Strickland, director, Office of Research Training and Special Programs; Katrin Eichelberg; Diane Adger-Johnson; and Raushanah Newman.

Mentoring Lecture Renamed in Honor of Hernandez

The late Dr. Milton J. Hernandez

NIAID's Bridging the Career Gap workshop mentoring lecture was recently renamed to honor Dr. Milton J. Hernandez, NIAID's former director of research training and strong supporter of new investigators. He died in 2012.

"Dr. Hernandez was sensitive to and active in addressing the challenges faced by scientists in the early stages of their careers," said Diane Adger-Johnson of the Office of Research Training and Special Programs. "Through his efforts, many new investigators successfully competed for NIH research training awards, helping launch their research and careers in the life sciences. Through his work in career development for young investigators, Dr. Hernandez inspired senior scientists to participate in the development of future scientific leaders. Naming this lecture for him is one way for us to honor his legacy."

The first Milton Hernandez Lecture of Excellence in Mentoring Life Sciences Researchers was presented recently by Dr. Derrick Brazill of Hunter College (mentor) and Dr. Kareem Graham of Emory University (protégé).

NIH Diet Plans Named Best, Once Again

By Jan Ehrman

Maybe the "N" in NIH should stand for nutrition.

Two diet plans developed by the National Heart, Lung, and Blood Institute have once again ranked atop a list of healthy diets created by a panel of nutrition and wellness experts overseen by *U.S. News and World Report*. This may be no surprise since NIH's location in Bethesda, home of more than 300 restaurants, makes food a local preoccupation.

For the fourth successive year, DASH (Dietary Approaches to Stop Hypertension) has been named the best overall diet. DASH was also deemed the optimal plan for those with diabetes and was noted in particular for its "nutritional completeness and safety."

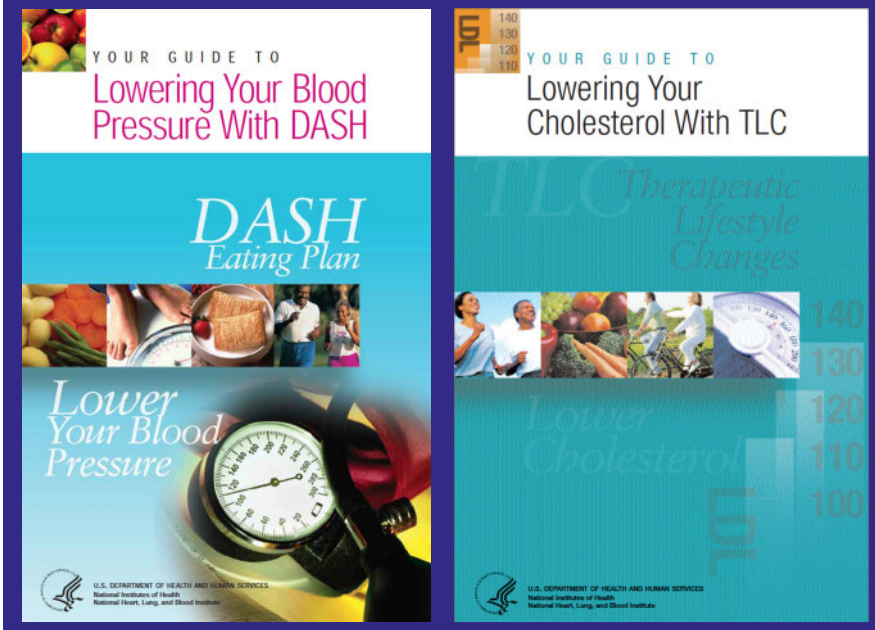
The TLC (Therapeutic Lifestyle Changes) diet placed second, for the second year in a row, in the category of best overall diets. This plan, noted for preventing cardiovascular disease, emphasizes consumption of foods that are low in saturated fats, trans fats and cholesterol. Both DASH and TLC have topped *U.S. News*'s rankings for the 4 years the magazine has rated diets.

One NIH nutrition expert explains that the DASH plan emphasizes eating foods good for you and avoiding ones that have little nutritional value. Additionally, there is no safety risk associated with the diet, according to Jody Engel of NIH's Office of Disease Prevention.

"Sit less and move more is a good prescription for everyone," said Jody Engel of NIH's Office of Disease Prevention.

"With the DASH diet, we are suggesting that people eat lots of fruits, vegetables, whole grains, low-fat dairy foods, as well as poultry, fish, meat, nuts and beans," said Engel. "Foods you should avoid or keep to a minimum include added fats, red meats and sugar-laden foods and drinks." Portion size is also important, as is obtaining the proper amount of nutrients, she added.

The TLC diet focuses on promoting cardiovascular health. The low-saturated fat, low-cholesterol diet aims at reducing blood cholesterol to a level that decreases the risk of heart disease. It suggests that daily cholesterol intake be kept below 200 milligrams and that sodium intake be limited to 2,400 milligrams per day. But diet is only one aspect. "The plan actually has three parts—diet, physical activity and weight management," said Engel, stressing that all are critical.



Two diet plans—DASH (Dietary Approaches to Stop Hypertension) and TLC (Therapeutic Lifestyle Changes)—developed by the National Heart, Lung, and Blood Institute have once again ranked atop a list of healthy diets created by a panel of nutrition and wellness experts overseen by U.S. News and World Report.

Evidence backs the two diets' efficacy and safety. "Since the 1990's, the benefits of both diet plans have been supported by numerous large research studies," said Shanna Bernstein, a Clinical Center dietitian. "These diets have been promoted by NHLBI and the National Cholesterol Education Program, among other professional organizations. Though each of the plans has a slightly different focus," she continued, "both emphasize foods that we know to be healthy such as fruits, vegetables and whole grains, while discouraging intake of high-fat meats and foods high in sodium."

She said positive results seen in research studies by those who adhere strictly to the diets suggest the regimens are applicable to the overall American population, regardless of race or body composition.

"'Diet' has become a four-letter word for many," said Lenora Johnson, communication director at NHLBI. "Yet, if we shift our focus from that which is quick or easy or fun to what research tells us really works, diets can be rewarding and life-changing experiences and synonymous with other four-letter words—live or life."

While neither diet gives carte blanche to cookies dipped in milk or large bowls of ice cream, both DASH and TLC potentially offer some degree of health benefit to almost everyone, especially when coupled with regular physical activity, according to the nutrition pros.

Notes Engel, "Exercise will help with weight reduction. It does not have to be a planned workout session. Sit less and move more is a good prescription for everyone."

Your Guide to Lowering Your Blood Pressure With DASH is available for download at www.nhlbi.nih.gov/health/public/heart/hbp/dash/new_dash.pdf; a 6-page summary can be downloaded at www.nhlbi.nih.gov/health/public/heart/hbp/dash/dash_brief.pdf.

To download *Your Guide to Lowering Your Cholesterol With TLC*, visit www.nhlbi.nih.gov/health/public/heart/chol/chol_tlc.pdf.