

ROBOTS + REHAB TRAINING

Can Exoskeletons Help Kids with CP Walk Better?

BY CARLA GARNETT

For more than a decade now, since 2008 when Marvel Studio's *Iron Man* debuted, pop culture fans have been fascinated by the idea of people donning robot parts to be stronger or faster. Medicine and technology teaming up to enhance physical ability is not new, either, with several generations of both theory and application finding success. Until recently, however, one population has been absent from the advances—children.

Enter Dr. Thomas Bulea, an engineer by training and staff scientist in Dr. Diane Damiano's functional and applied



Dr. Thomas Bulea presents at CC Grand Rounds.

biomechanics section in the Clinical Center rehabilitation medicine department. A few years ago, Bulea led an effort to explore the role of exoskeletons for pediatric patients. He described their progress at a

recent CC Grand Rounds lecture, "Robotic Exoskeletons for Improved Walking in Children with Cerebral Palsy."

First, a short primer on cerebral palsy (CP). CP refers to a group of neurological disorders that stem from damage to or under-developed parts of the brain. It's usually diagnosed at birth or by age three.

"A hallmark of CP," Bulea said, "is abnormal motor control due to spasticity and muscle contractures resulting in diminished coordination in both upper and lower extremities."

A common walking disorder that people with CP experience is crouch gait, characterized by excessive bending of the limb, or flexion, especially at the knee. The hip and ankle may also be involved, and CP can affect one or both sides of the body.

"Biomechanically," Bulea explained, "a person with crouch gait walks with one or

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White House science chief visits. See story, p. 9.

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Manji Develops Novel Treatment for Major Depressive Disorder

BY DANA TALESNIK

Major depressive disorder is a debilitating, chronic disease that afflicts more than 300 million people worldwide, one-third of whom don't improve after trying different antidepressants. At long last, many in this cohort of treatment-resistant patients may soon find some relief.

Dr. Husseini Manji, global head of



Dr. Husseini Manji

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Curlin Presents Alternative View of Patient-Clinician Dialogue

BY MOHOR SENGUPTA

As the Clinical Center buzzes with everyday activity, there sometimes comes that snag clinicians face while informing a patient that his or her chosen course of treatment is not the best one, even though the patient consented to it.

A recent CC Ethical Grand Rounds talk hosted by Dr. David Wendler, senior



Dr. Farr Curlin

SEE CURLIN, PAGE 8

Employee Survey Opens, Ends July 1

The 2019 Federal Employee Viewpoint Survey (FEVS) is scheduled to open on Monday, May 20 and will remain open for a 6-week period closing on Monday, July 1.

This is your opportunity to provide input on a variety of topics within your organization, including work experience, leadership, diversity and inclusion. Your candid input helps make NIH a more engaging and fulfilling place to work.

NIH values your feedback and uses the survey results to make positive changes throughout the organization. FEVS is one of the fundamental ways the NIH community learns how to improve as a place to work and as an agency that sets standards of excellence in medical research.

The Office of Personnel Management sends an email invitation with a unique link to all eligible NIH employees (full- and part-time permanent, non-seasonal employees, on board on or before Oct. 27, 2018). The survey takes 20-25 minutes to complete and responses are confidential.

In 2018, NIH reached its highest participation rate to date with 62.2 percent of all federal employees completing the survey (5.1 percentage points higher than 2017). This year, NIH hopes to sustain its increasing participation rate to ensure even more employees' voices are heard.

For questions about FEVS, visit <https://hr.nih.gov/fevs> or contact the Office of Human Resources at NIHFEVS@nih.gov.

NIMH's Berman To Give Roberts Lecture

May 30

NIMH's Dr. Karen Berman will give the 2019 lecture in the Anita B. Roberts Lecture Series honoring Distinguished Women Scientists at NIH, sponsored by the NIH women scientist advisors committee. Her talk "Williams Syndrome: A Rare View of the Path from Genes to Neural Circuits to Behavior and Back Again," will be held on Thursday, May 30 from 1 to 2 p.m. in Lipsett Amphitheater, Bldg. 10.



Berman is a senior investigator and chief of the Clinical and Translational Neuroscience Branch, the section on integrative neuroimaging and the psychosis and cognitive studies section. She conducts translational investigations, using multimodal neuroimaging to bridge the gap between neurogenetic, molecular, cellular and system-level mechanisms in neurodevelopment and in neuropsychiatric disorders.

Berman completed residency training in psychiatry

at Washington University in St. Louis and at the University of California at San Diego, as well as a residency in nuclear medicine at the Clinical Center. She has board certification in both psychiatry and nuclear medicine.

The seminar series is dedicated to the memory of Roberts, former chief of NCI's Laboratory of Cell Regulation and Carcinogenesis from 1995 to 2006.



NIDA, NIAAA, NIMH Host Diversity Workshop

The directors of the National Institute on Drug Abuse, National Institute on Alcohol Abuse and Alcoholism and National Institute of Mental Health hosted and provided welcoming remarks at the Diversity Supplement Professional Development Workshop on Apr. 8-9 at Neuroscience Center headquarters in Rockville. The workshop brought together more than 40 diversity supplement scholars from all three institutes to showcase their research, hear from the institute directors and get professional development training. Above, NIMH director Dr. Joshua Gordon offers remarks at the workshop. For more pictures, visit <https://flic.kr/s/aHsmh8AVen>.

The lecture is open to all and will be followed by a reception with refreshments. For sign-language interpretation, email mmcburney@od.nih.gov or call (301) 496-1921.

Two NIDA intramural staff members, Dr. Rao Rapaka and Dr. Roger Sorensen, received awards at the Society of Neuroimmune Pharmacology's

25th annual scientific conference Apr. 10-13 in Portland, Ore.

NIDA Staff Honored for Addiction Research

Rapaka, chief of the Chemistry and Pharmacology Branch, won the Lifetime Achievement Award for his dedication and visionary outlook in creating new directions for research in drug use and his vision in bringing cutting-edge advances in the fields of lipidomics. He was also cited for his passion for mentoring scientists, paving the way for seminal discoveries in new approaches, targets and medications in development for drug use pharmacotherapy.



Dr. Roger Sorensen (c) accepts his Outstanding Service Award in the company of NIDA's Dr. Woody Lin (l) and Dr. Johnny He, outgoing SNP president.



Dr. Rao Rapaka displays his award.

Because of his research, Rapaka also received the Lifetime Achievement Award from the University of Arizona during a symposium on the neurobiology of pain and addiction held Apr. 24.

and addiction.

Mooney Describes How to Tune Up Tissue Regeneration

BY CATHERINE EVANS

Regenerative medicine researchers can envision a not-too-distant future when stem cells help to treat periodontal disease, broken jaws, craniofacial defects and more. But first, several challenges must be addressed. For one, it's not effective to simply inject a mass of stem cells into damaged tissue. Without a physical scaffold to hold cells in place and chemical cues to prompt repair of a defect, stem cells drift away or die.

To address this problem, scientists in the lab of Harvard bioengineering professor Dr. David Mooney design gel-like materials called hydrogels that mimic stem cells' natural environments. At a recent NIDCR Grand Rounds in Lipsett Amphitheater, Mooney described how hydrogel-encapsulated stem cells can be more precisely controlled, whether grown in the lab or injected into the body.

Years of investigation have shown Mooney's group that the mechanical properties of a hydrogel—its stiffness or stretchiness—profoundly influence whether bone marrow-derived stem cells (mesenchymal stem cells) develop into fat or bone.

"Mechanical cues can regulate the formation and remodeling of tissues," said Mooney. "We're looking at how we can use the mechanics of the substrate to regulate stem cell behavior in the context of regeneration."

Mimicking the Matrix

In adults, many factors dictate whether stem cells stay on their home turf or move to a site of injury. These instructions come from growth- or healing-related molecules, contact with neighboring cells and attachment to the extracellular matrix, a 3-D fibrous network that supports cells and gives shape to tissues and organs. As stem cells grow, divide and meander, they are in constant contact with the extracellular matrix. Cells inevitably push against the matrix, and like a rubber band, the matrix pushes back.

"Our approach is to try to understand the signals cells receive in their home environments and build them into our biomaterials," explained Mooney.

Scientists in Mooney's lab nearly a decade ago wondered if the stiffness of a hydrogel's matrix—its elasticity—could affect stem cells. The researchers crafted hydrogels using alginate, a complex sugar that gives seaweed its structure and flexibility. Chemical tweaks to the alginate enabled the scientists to adjust hydrogel elasticity and study its effect on cells.



Dr. David Mooney described how biomaterial mechanics affect tissue regeneration at a recent NIDCR Grand Rounds.

PHOTO: ELIZA GRINNELL

The Mooney group found that mouse and human mesenchymal stem cells grown in softer hydrogels developed into fat-forming cells. In stiffer hydrogels, the cells became bone-forming cells. Hydrogel elasticity also affected the extent of bone regeneration in rat skull defects—medium stiffness worked best. It seemed that matching a hydrogel's stiffness to that of a given tissue—fat or bone—could nudge cells to form that tissue. The stiffest hydrogels were least effective, perhaps because they were too confining to cells.

"Simply by adjusting the mechanical properties, we can control stem cell behavior and regeneration not only in culture, but also *in vivo*," Mooney said.



"Our approach is to try to understand the signals cells receive in their home environments and build them into our biomaterials."

—DR. DAVID MOONEY



But elasticity was only part of the story. "Our studies ignored some key aspects of biology," Mooney said. "When stretched, tissues such as fat, liver and brain don't snap back into shape like a rubber band. Instead, they have properties between a liquid and a solid—they're viscoelastic."

To find out if viscoelasticity affects cells, the Mooney team developed gels with both elastic and viscoelastic features. Such materials initially

respond elastically to an applied force. But if that force persists over time, instead of snapping back into shape, viscoelastic materials spread and creep and lose their original shape, similar to modeling clay.

The researchers found that specific levels of both elasticity and viscoelasticity governed whether mesenchymal stem cells grew into bone- or fat-forming cells or healed skull bone defects in rats.

"Our hydrogel is an important tool to study, in a tightly controlled manner, how cell fate is regulated during development, pathology and regeneration," Mooney said. "This research may also allow us to intervene in new ways by altering the mechanical cues cells receive in order to enhance healing and limit disease progression." **R**



ON THE COVER: Stem cells engineered to grow cartilage. A scaffold was shaped over a mold, attached to mesh and seeded with stem cells. After 38 days in culture, the stem cells had grown to create a smooth, glistening surface. This process may lead to treatments for hip osteoarthritis that avoid the need for extensive hip replacement surgery.

IMAGE: GUILAK LAB, WASHINGTON UNIVERSITY WITH FUNDING FROM NIAMS

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Depression

CONTINUED FROM PAGE 1

neuroscience at Janssen Research & Development, LLC, one of the Janssen Pharmaceutical Companies of Johnson & Johnson, has pioneered a ketamine-based nasal spray that, in multiple clinical trials, has swiftly alleviated depressive symptoms in patients who have not responded to other medications. This treatment, the first neuroscience drug to receive “breakthrough therapy” designation from the Food and Drug Administration, is the first new treatment for major depressive disorder in decades.

Just days before esketamine nasal spray would receive FDA approval, Manji spoke at an NIMH Director’s Innovation Speaker Series lecture in the Neuroscience Center.

“Developing a new medication for anything is very, very difficult,” said Manji, a former NIMH fellow, lab chief and director of NIH’s Mood and Anxiety Disorders Program. “Drug failure rates are in the 90-plus percent range. For complex neuropsychiatric conditions, [the failure rate] is even worse.”

Yet there’s an enormous need for better treatments. Mental illnesses tend to strike people when they’re young and the conditions are so incapacitating because they’re generally lifelong, said Manji. Across North America and Europe, “We were struck to find mental illnesses were the most disabling conditions in the 15-44 age group,” he said.

In the United States, major depression has become the leading cause of disability and can be fatal. Suicide claims the lives of more than 45,000 Americans annually.

Despite the need for new therapies, many pharmaceutical companies have abandoned the mental health field altogether, investing instead in other areas that have higher success rates. As mental illnesses become more pervasive, Manji and his team remain determined to find solutions.

The drug ketamine, a powerful anesthetic, has been studied for some time for its antidepressant properties. The drug works by disinhibiting certain neurons while triggering others. In clinical trials in the early 1990s, many patients responded quickly to low-dose ketamine administered intravenously.



Manji wanted to find a way to help millions and started thinking about a more expedient delivery method than IV infusion. When he arrived at Janssen, he wondered, “Is there a way we can make this a safe, effective, FDA-approved convenient medication?”

As they began to explore an intranasal version, they searched for a potent form of ketamine that might work with the tiny volume emitted by a nasal spray. Esketamine showed rapid and robust antidepressant effects at a low dose. Encouraged to see patients improve quickly, Manji and his team also wanted to explore how to keep them better longer.

“What drug do we have that a single dose lasts forever?” he asked. Surprisingly, though, they found a single dose helped keep people well for several days.

The strategy was to give patients esketamine twice a week for the first month, then administer the treatments every 1-2 weeks to help maintain the effects. After conducting a series of clinical trials, including 6 phase-3 studies, the positive data generated from 1,700 patients led to the treatment’s FDA approval.

“Our data showed,” said Manji, “that with intranasal administration, we can get treatment-resistant depressed patients better faster and, with intermittent dosing, keep them well.”

Ketamine has serious side effects—and some abuse potential—so even the nasal spray version is not a take-home drug. Esketamine must be administered in a clinic under a health care professional’s supervision. The two major side effects—hallucinations and increased blood pressure—usually peak within 30-40 minutes and disappear shortly after, explained Manji. The patient remains at the clinic for a couple of hours after treatment for monitoring, then gets discharged but is not permitted to drive for the rest of the day due to the drug’s drowsy effects.

“If this is going to be a life-saving, life-altering treatment,” Manji said, “let’s make sure we do it correctly.”

Whereas other treatments can take weeks to work, esketamine is effective within hours and can be useful in acute crisis. The rapid response is particularly important for helping those at imminent risk of suicide. There are ongoing phase-3 studies of this second proposed indication for esketamine. Also encouraging, long-term studies consistently showed that patients had a significantly reduced risk of relapse with intermittent esketamine treatment.

Developing treatments for mental illness involves a complex web of advanced genetics, protein engineering, biomarker identification, neuroimaging and data mining. These are diseases of synapses and circuits, said Manji, so it’s possible to make advances by finding and manipulating the right pathways, even if every gene involved can’t yet be identified.

Within that circuitry, AMPA (alpha-amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid) receptors, which are found all over the brain and regulate excitability, remain an ongoing area of research.

“We think AMPA receptors, being so ubiquitously expressed, are going to lend themselves to novel therapeutic development,” said Manji. “We now have novel ways to target them in specific circuits, rather than throughout the brain.”

We need a massive effort, he said, in which scientists, advocates, companies and the government come together to address mental illness. “I think if we can work together as a society, we can make a big difference for our patients.” **R**

Innovations in Technology to Extend the ‘Golden Hour’

BY RAYMOND MACDOUGALL

The “golden hour” is a concept in trauma care medicine that describes the critical first hour after a life-threatening injury, when medical and surgical interventions may determine a patient’s survival. At a recent workshop, civilian and military clinicians and bioengineers met at NIH to consider a roadmap for “Innovations in Technologies to Extend the Golden Hour.”

“Trauma is the leading cause of death in people under the age of 40 years in developed countries,” said co-organizer Dr. Seila Selimovic, director of NIBIB programs in biosensors and tissue engineering, noting that proximity to medical facilities can make a big difference in outcomes. “An injured person in an urban environment may be able to reach an emergency room within 20-30 minutes, while a person living in a rural environment may not reach a hospital for a full hour after the injury.” The time that elapses prior to reaching a hospital becomes longer in natural disasters and for soldiers on the battlefield, she said.

The workshop is among the first to engage civilian and military experts in promoting innovation of technologies to extend the golden hour. Bioengineered solutions hold promise for improved diagnostic treatment of acute injuries and shock, to increase survival and recovery rates. New technologies have been introduced in recent years, many pioneered in battle in Afghanistan and Iraq. Others face technical, financial or logistical obstacles before their potential to save lives is realized.

“The future of medicine is about continuous dynamic biology, and it requires continuous sensing, feedback and control systems—technologies that we love to apply in engineering,” said NIBIB director Dr. Bruce Tromberg. “This is essential for advancing the future of medicine in general, and I think it is going to be leveraged beautifully into advancing what we can do in that golden hour.”

Some examples of biomedical technologies already used in critical care include tourniquets; hemostatic agents, which are applied to trauma pads and combat gauze to stanch hemorrhages; organ support



Meeting organizer Dr. Seila Selimovic with NIBIB director Dr. Bruce Tromberg

PHOTO: RAYMOND MACDOUGALL

technologies such as tracheostomy tubes, ventilators and dialysis systems; non-invasive imaging for burn patient care; and wearable sensors to monitor heart and breathing rates and to prompt caregivers.

Dr. Thomas Scalea, physician-in-chief at the University of Maryland Shock Trauma Center, said the golden hour doesn’t always equal a 60-minute window; rather there are many time-sensitive aspects to treating a living patient in real time. These include airway control, blood loss, brain injury, fractures and weak blood circulation. “Extending the golden hour doesn’t mean doing the same things faster,” he said. “This involves taking the therapy out of the emergency department and into the field.”

Battlefield medicine should not be overlooked in importance for a modernized military, according to Col. Michael Davis, a physician who directs the U.S. Army Medical Research and Materiel Command’s Combat Casualty Care Research Program. “Military medicine faces a crisis of relevance,” he said. “We have to educate and inform [leadership] about how important medical care is to winning on the battlefield.”

After an overview of civilian and military needs, breakout groups focused on organ support technologies; radiation exposure/burn and wound-healing; hemostatic medical devices; portable imaging technologies; and wearable biosensors. The workshop will be summarized for the potential of further collaboration and priorities for trauma care research. **R**

NINR’s Cashion Discusses ‘Future of Nursing’

NINR acting director Dr. Ann Cashion was one of several nursing organization leaders invited to present comments recently at the public session for the Committee on the Future of Nursing 2020-2030. The committee, sponsored by the Robert Wood Johnson Foundation under the auspices of the National Academies of Sciences, Engineering, and Medicine, will examine current and future challenges in developing its recommendations for nursing in the next decade.

Cashion noted that nursing science’s primary focus is on improving the quality of a person’s life at any age—not necessarily on curing disease. Describing NINR-supported science in key research areas such as symptom science, wellness, self-management and end-of-life and palliative care, she highlighted the work of NINR scientists who discovered biomarkers of neuronal damage in athletes and military personnel following traumatic brain injury, and who developed early palliative care interventions tailored to patients with newly diagnosed incurable cancer.

“We are very proud of the contribution that nursing science has made to improving health and to supporting the nursing field, and we are excited about what can be achieved in the future,” said Cashion. She urged the committee to highlight the importance of nursing science in advancing nursing, with a specific call for more Ph.D.-trained nurses.



ORWH Meeting Features Volkow

The Office of Research on Women’s Health hosted the 48th meeting of its advisory committee on research on women’s health on Apr. 10 at Natcher Conference Center. Dr. Nora Volkow (above), director of the National Institute on Drug Abuse, gave the keynote address. She described the Helping End Addiction Long-Term (HEAL) Initiative and NIDA-supported research addressing sex differences in pain and addiction. Launched a year ago, the HEAL Initiative builds on NIH research on pain and addiction and on integrating behavioral interventions with medication-assisted treatment to improve treatments for opioid use and addiction and to enhance pain management. You can view the meeting at <https://videocast.nih.gov/> and read more information at <https://orwh.od.nih.gov/advisory-committees/acrw/>.

Exoskeletons

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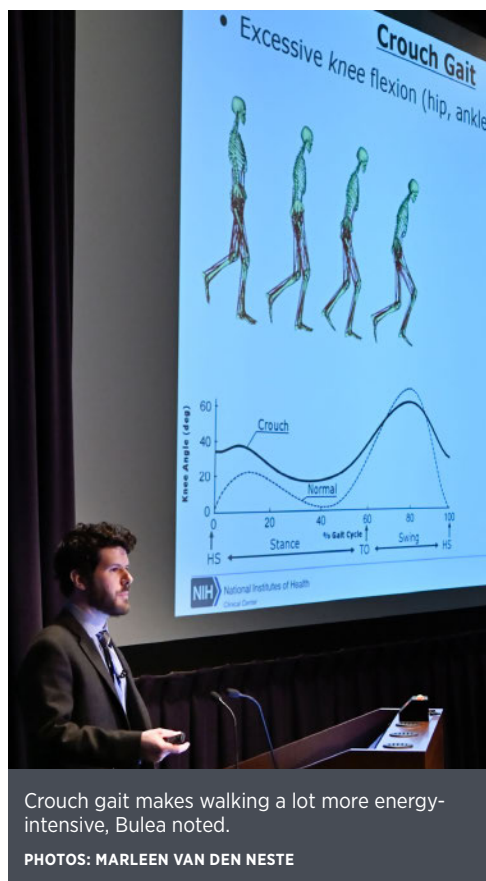
both knees bent. The leg never straightens completely as in a normal stride, and the limb's range of motion is limited."

Crouch gait makes walking a lot more difficult and energy-intensive, he noted.

"Children with crouch have to counteract flexion moments due to gravity with internal moments generated by their own muscles," Bulea said. "As a result, they have to exert a lot more energy to maintain upright posture than individuals without crouch. Also, the muscles themselves are in a biomechanically less favorable position to extend the limb, so they need to work even harder to provide the necessary extension support."

It's a difficult cycle that leads to future problems: Kids with CP have to use more energy to move; muscles therefore become fatigued faster, and that leaves the children less likely to move.

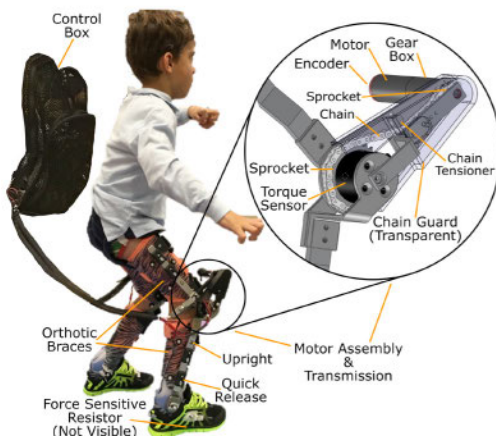
"Studies show that children with CP spend less of their time at high-activity levels, so they're less active than their typically developing peers," Bulea explained. "These periods of activity are important for



Crouch gait makes walking a lot more energy-intensive, Bulea noted.

PHOTOS: MARLEEN VAN DEN NESTE

1st Generation



2nd Generation



Bulea and colleagues have fine-tuned the exoskeleton's design, streamlining several features to make it more compact, portable and less cumbersome.

IMAGE: THOMAS BULEA

development of children's muscle strength and coordination. Thus, children with CP do not experience sufficient muscle strength development, especially during periods of rapid growth."

Consequently, there's a natural progression (or increase) of crouch gait as kids with CP age.

"Roughly half of children who are ambulatory as adolescents lose the ability to walk in adulthood," he said.

Treatments for crouch gait vary and come with drawbacks:

- The most popular—and also most invasive—intervention is surgery to lengthen the hamstring and improve knee extension.
- Strengthening via physical therapy often has only short-term effectiveness.
- Botulinum toxin injection to ease overactivity of knee flexor muscles typically wears off after 4 to 6 months.
- Orthotic devices correct posture, but also can worsen weakness over time.

"There really is no effective long-term solution for treatment of crouch gait," Bulea said.

That's what prompted the group to pursue robotic-assisted gait training.

"We set out to design an exoskeleton from the ground up specifically for children with cerebral palsy and, even more narrowly, children with crouch gait from cerebral palsy," he said.

They invented a kid-sized exoskeleton device that helps children walk, but also trains them to walk better on their own.

"Training has to be both engaging and

challenging," Bulea pointed out. "We like to think of successful rehabilitation as a form of motor learning, and these are key elements. The prevailing approach has been to use an assist-as-needed control strategy whereby the robot adjusts its assistance force based on the volitional action of its user."

The goal, he said, was to make a device

★ ★ ★

"Exoskeletons allow us to transition gait training out of the clinic and into the community."

-DR. THOMAS BULEA

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that functions in two ways. First "we wanted to make it a little easier for these kids to walk so that they'll walk more." The second goal was to "change the way they use their muscles to walk while they're wearing it, with the hope that these changes will eventually translate to when they walk without the exoskeleton."

Unlike assist-as-needed robotic gait training that imposes a predefined trajectory, the user-driven device actually tracks and responds to the user's own activity, Bulea explained. We wanted to create "a new paradigm for how this robot would interact with children while they are wearing it."

Adaptation concepts were applied to the device's design and its assistance features synchronize with the actions of the user.

The group tested the first model of the device in a 6-visit clinical study of 7 male and female young people, ages 5 to 19 years. Although designed simply to test safety and feasibility of the new approach, the study garnered several positive results.

Users' crouch gait improved in the first session with the device. But perhaps more importantly, performance continued to improve as kids moved through the study. Walking with the exoskeleton significantly reduced asymmetry and over time users walked even better.

What's more, Bulea reported, the device preserved autonomy. "We saw that the kids were not letting the robot do the work for them."


Bulea and colleagues have since fine-tuned their design, streamlining several features to make it more compact, portable and less cumbersome.

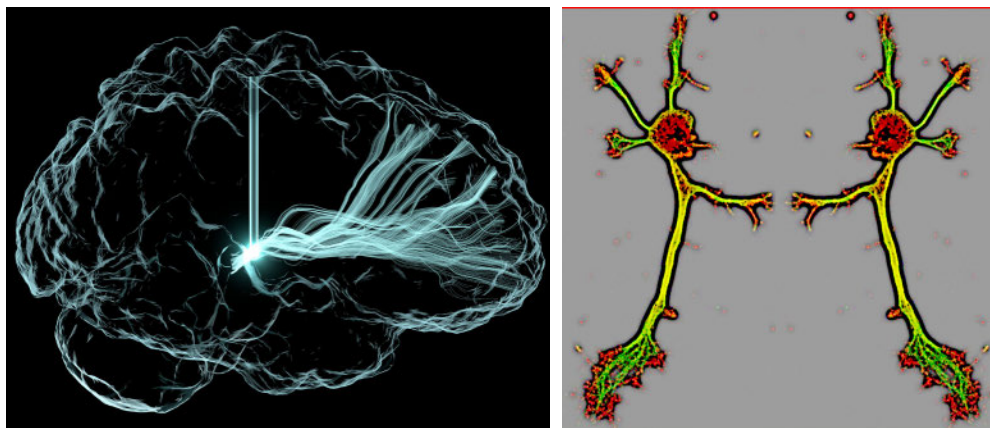
"We don't envision that this exoskeleton would be a stand-alone solution," he said. "We envision it as something clinically that's used in combination with other treatments."

Immediate next steps include expanding the user base for the technology, getting it to younger individuals and to populations beyond people with CP such as children with spina bifida, incomplete spinal cord injury or muscular dystrophy.

The group is also working on a tablet-based interface for parents or physical therapists to use with kids and looking into neuro-imaging technology so researchers can see the brain activity that underlies some of the movements users make while wearing the device.

In addition, Bulea and the team have integrated the exoskeleton with other technology to make the rehabilitation/training environment more engaging. Debut of the video gaming—"exer gaming"—application was a hit with both its target audience and some adults as well.

"Exoskeletons allow us to transition gait training out of the clinic and into the community," Bulea concluded. "That has a lot of powerful implications, with perhaps the most important being the ability to greatly increase the dosage and intensity of training. Rather than coming into a clinic once or twice a week for gait training on a treadmill, children can train for hours a day everyday for months or years." 



1st place "Light Me Up!" (l) by Andrew Janson and 2nd place "Dancing Devils" by Dr. Sharada Tilve

BRAIN Initiative Contest Garner Eye-Catching Photos, Videos

Neuroscience imagery has come a long way since the hand-drawings of Spanish scientist-artist Santiago Ramón y Cajal. Yet, images, and now videos, continue to capture the wonder and beauty natural to the exploration of the brain.

NIH recently hosted its first-ever BRAIN Initiative "Show Us Your Brains!" Photo and Video Contest as a fun way to showcase and demonstrate to the public the creativity and artwork of scientists working on the BRAIN Initiative.

The contest was held as part of the 5th annual BRAIN Initiative Investigators Meeting Apr. 11-13 at Washington Marriott Wardman Park Hotel in Washington, D.C. Cool, eye-catching image submissions were encouraged from anyone engaged in the initiative, regardless of discipline, career stage or funding source.

The program committee reviewed a total of 58 submissions—36 photos and 22 videos—and selected entries they felt best captured the creative spirit of the initiative. Those images then were posted online for public voting; the winning top 3 photos and top 3 videos were announced Apr. 13.


Contest winners are listed below. To view the full group of winning images, visit <https://bit.ly/2Un2xnX>.

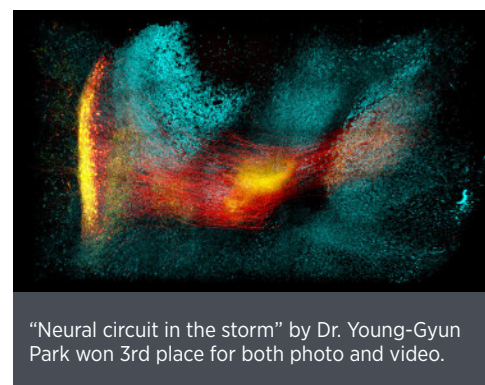
Photo Winners:

- First Place: "Light Me Up!" from Andrew Janson, graduate student research assistant, Scientific Computing and Imaging Institute, University of Utah. Light-based rendering of deep brain stimulation's electrical excitation of neuronal fiber pathways to treat patients with traumatic brain injury.
- Second Place: "Dancing Devils" from Dr. Sharada Tilve, postdoctoral fellow, Geller Lab Group, NHLBI. Mouse hippocampal neuron stained for f-actin (red) and tubulin (green) look like the devil dancing ballet.

- Third Place: "Neural circuit in the storm" from Dr. Young-Gyun Park, postdoctoral fellow, Chung Lab, MIT. 3-D image of parvalbumin+ neurons (red, neurites; green, presynaptic puncta) swimming through the waves of GAD1+ (cyan) neurons.

Video Winners:

- First Place: "High-Resolution MORF3-labeled Hippocampal Neurons" from Dr. X. William Yang, UCLA and Dr. Kwanghun Chung, MIT. Using MORF3 and SHIELD, pyramidal neurons were sparsely labeled and imaged at very high resolution deep within a whole hemisphere.
- Second Place: "3-D Diffusion Tractography" from James Stanis, medical animator, Mark and Mary Stevens Neuroimaging and Informatics Institute, USC.
- Third Place: "Neural circuit in the storm," which placed in both categories. 



"Neural circuit in the storm" by Dr. Young-Gyun Park won 3rd place for both photo and video.

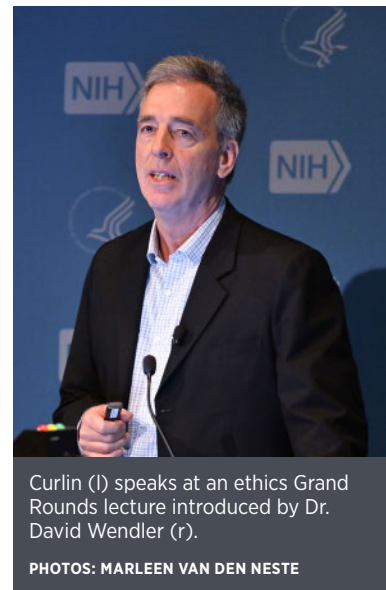
Curlin

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investigator and head of the section on research ethics in the hospital's department of bioethics, addressed the dilemma faced by clinicians trying to change a patient's informed decision. The situation is even more complex when the decision is based on a patient's religious beliefs.

To get an idea of how unusual some informed choices seem to a clinician, consider the case of BB, a woman with three grown children, plenty of friends and an active social life even after twice overcoming cancer. BB visited the Clinical Center when her cancer came back for a third time and had metastasized. The oncologist gave her three options. One, a phase-3 clinical trial that had shown promising results in many patients; two, a phase-1 clinical trial that was in its earliest stage and was predicted to be very toxic to BB; and three, symptomatic treatment at home, which meant enjoying her remaining days without any remedial intervention.

BB chose option two. She said that having fully understood the implications of a new and untested clinical recourse, she felt, as a



Curlin (l) speaks at an ethics Grand Rounds lecture introduced by Dr. David Wendler (r).

PHOTOS: MARLEEN VAN DEN NESTE

“Because of these concerns, physicians are generally discouraged from crossing over this boundary between religion and medicine,” said guest speaker Dr. Farr Curlin, the Josiah C. Trent professor of medical humanities, palliative medicine specialist and ethicist at Trent Center for Bioethics, Humanities & History of Medicine at Duke University Divinity School.

“Over the past half century, multiple

of medical science into the reflective and personal realm of religion found the experience to be deeply rewarding.

Patients have not only been responsive but also appreciative and grateful for having religious or spiritual discussions with their caregivers, even if they did not share the same religious belief, Curlin and his colleagues observed in an inpatient study at the University of Chicago. Even those who did not actively seek spiritual discussions, but were somehow led into it, found their hospitalization experience more satisfying than those who did not have such discussions at all.

After years of experience as a palliative care practitioner and ethicist, Curlin advises physicians to disregard the medicine-spirituality boundary in doctor-patient dialog. He observed that current norms emphasizing competence, autonomy and neutrality are only fitting if discussions about spiritual concerns are some form of “technique” applied by one stranger to another.

Better norms, he suggested, are wisdom—which develops with experience and is shown in good clinical judgment; respect—which is shown in taking a patient seriously; and candor—which means being honest about disagreements. These norms fit conversations governed by solidarity between the patient and physician.

Finally, says Curlin, “Once you have concluded that there are a number of reasonable ways forward that you’d support, you’ve got to respect the patient’s authority to choose among them.” **R**

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“Over the past half century, multiple movements have emphasized that patients’ experiences of illness are shaped by their particular histories and cultures.”

-DR. FARR CURLIN



devoutly religious individual, that God was looking out for her and that she wouldn’t experience the potential side-effects of the phase-1 medication. The perplexed oncologist, who happened to be an atheist, contacted the bioethics team for help.

Modern ethical norms of clinical trials tend to be straightjacketed by boundaries of physician practice. There is emphasis that a physician must be competent to understand a patient’s choice, should never infringe upon the patient’s autonomy in choosing a treatment and be neutral towards his or her own and the patient’s spiritual beliefs.

movements have emphasized that patients’ experiences of illness are shaped by their particular histories and cultures,” said Curlin. Likewise, “clinicians are trained to resist the undue influence of their so-called personal values.” However, this conventional narrative doesn’t always describe the reality.

Most physicians are wary of discussing spiritual matters with their patients and actively avoid such issues when brought up by the patient, according to studies conducted by Curlin and his colleagues. But those few who did cross the boundary from the logical and impersonal landscape



NIH director Dr. Francis Collins and OSTP director Dr. Kelvin Droegemeier on opposite sides of conference table, surrounded by staff including (from l) NIGMS director Dr. Jon Lorsch, NIH associate deputy director Dr. Tara Schwetz, principal deputy director Dr. Lawrence Tabak, acting chief of staff and NIH associate director for science policy Dr. Carrie Wolinetz and NIBIB director Dr. Bruce Tromberg



Droegemeier looks through a microscope in the laboratory of Dr. Steve Rosenberg, who discussed innovative cancer immunotherapies, including CAR-T cell therapy.



Droegemeier addresses IC directors and NIH senior leadership in Bldg. 1.

President's Science Adviser Visits Campus

Dr. Kelvin Droegemeier, director of the Office of Science and Technology Policy—and thereby the President's science adviser—visited NIH on Apr. 18.

The morning-long visit included a meeting with institute directors and senior NIH leadership in Bldg. 1, then a tour of the Clinical Center.

Stops there included a briefing with Dr. Steve Rosenberg, chief of NCI's Surgery Branch, and a tour of the special clinical studies unit, led by NIAID director Dr. Anthony Fauci.



Clinical Center CEO Dr. James Gilman (r) shows Droegemeier a model of the Clinical Research Center.



Droegemeier (l) visits the special clinical studies unit with Fauci (c) and Dr. Richard Davey (third from r), who runs the unit.

PHOTOS: CHIA-CHI CHARLIE CHANG



Collins (c) chats with Droegemeier. At the table are (from l) NIDDK director Dr. Griffin Rodgers, NIAID director Dr. Anthony Fauci, Tabak, Wolinetz and NLM director Dr. Patricia Brennan.

NRC Commissioner Visits NIH

On Apr. 17, NIH hosted a visit by Nuclear Regulatory Commissioner David Wright, who toured several clinical areas as part of his “get out and meet the licensees” initiative. As a cancer survivor, he was particularly interested in visiting the NIH program and seeing how radiation and radioactive materials are used for cancer research.

NIH Radiation Safety Officer Cathy Ribaldo of the Division of Radiation Safety, ORS, organized the tour. Stops included a kick-off meeting with Clinical Center CEO Dr. James Gilman, the hospital’s nuclear medicine and PET departments, the department of transfusion medicine, NCI’s Ex-Vivo Laboratory and the Molecular Imaging Program.

Multiple clinicians took the time to explain their research and showcase the innovative uses of radioactive material at NIH, as well as discuss some novel cancer research applications. Wright was delighted with everything he saw, Ribaldo reports.

The final tour stop was Bldg. 1 for a meeting with Dr. Alfred Johnson, NIH



On hand at the visit were (clockwise from l) Lisa Coronado, Office of Intramural Research; NIH deputy director for intramural research Dr. Michael Gottesman; Dr. Brad Wood, chief, interventional radiology, CC; Dr. Richard Wyatt, deputy director, Office of Intramural Research; Cathy Ribaldo, ORS; NIH deputy director for management Dr. Alfred Johnson; NRC Commissioner David Wright; and NRC staffers Samantha Crane and Jan Nguyen.

deputy director for management, Dr. Michael Gottesman, NIH deputy director for intramural research and OIR deputy director Dr. Richard Wyatt. Wright shared

his gratitude and favorable impressions of his NIH visit and committed to continuing his advocacy work on cancer awareness and education. **R**

NICHD Engages with Community at Forum

NICHD director Dr. Diana Bianchi (seated, r) joined panelists at NICHD’s Community Engagement Forum on Improving Maternal Health on Apr. 8. The group discussed rising U.S. maternal mortality and morbidity rates and solutions. Participants included (standing, from l) Dr. Shavon Artis Dickerson, NICHD; Dr. Sonia Hassan, Wayne State University School of Medicine; Tesheia Johnson, Yale Center for Clinical Investigation; Kay Matthews, Shades of Blue Project; Angela Doyinsola Aina, Black Mamas Matter Alliance; Dr. Haywood L. Brown, University of South Florida; Dr. Melissa Kottke, Emory University; and Dr. Charisee Lamar, NICHD. Seated are (from l) Peggy Gautreau, National Association of Rural Health Clinics; Jennifer Senda, National Research Center for Parents with Disabilities; and Robyn D’Oria, Central Jersey Family Health Consortium.



Webinar Features NIDA Deputy Director

Dr. Wilson Compton, deputy director of the National Institute on Drug Abuse, was a featured speaker at a webinar sponsored by the Providers Clinical Support System and the American Dental Association on Apr. 3. He joined colleagues Dr. Martha Somerman, director, National Institute of Dental and Craniofacial Research, and Dr. Brad Rindal, senior research investigator and associate dental director for research, HealthPartners Dental Group.

Coordinated by NIDA’s NIDAMED program, speakers presented an overview of the opioid crisis, how addiction is a chronic brain disease and how NIH is addressing the issues through research. It recognized the challenges associated with dental procedure pain management in the context of the opioid crisis, addressed the efforts of the HEAL Initiative and discussed ongoing and completed studies related to dental pain management and opioid prescribing studies.

Just over 1,000 dentists participated in the webinar. NIDAMED coordinates the development and dissemination of science-based resources to health care providers nationwide.



NIH Patient Lee's Legacy Lives On

NIH mourns the passing of Andrew Lee, 23, who died on Apr. 21 following a hard-fought battle with cancer.

In 2015, after finishing his freshman year of college, Lee was diagnosed with stage 4 HLRCC (hereditary leiomyomatosis and renal cell cancer), a rare form of kidney cancer with no known cure. Determined to fight the terminal disease and contribute to research, Lee would participate in seven NIH-led clinical trials, including collaborations with Yale and Georgetown cancer centers.

Family and friends described Lee, of Kensington, Md., as a caring, positive person with a quiet resilience. He remained optimistic during his treatments and rarely complained, despite unrelenting pain and other serious symptoms and side effects.



Driven to Cure founder Andrew Lee raised more than \$400,000 for cancer research.

doing everything he could to help other patients with this disorder.”

Soon after his diagnosis, Lee's father bought him his dream car, a Nissan GT-R, which he turned into a fundraising vehicle.

In 2016, Lee founded the nonprofit Driven to Cure to raise awareness and research dollars for rare kidney cancer. He took his customized GT-R to auto shows in between cancer treatments, raising more than \$400,000 for the Foundation for the NIH to fund kidney cancer studies at the Clinical Center.

Lee received multiple awards from FNIH for his unwavering commitment to biomedical research. In addition to his fundraising efforts, Lee also donated his kidney and tissues to NIH to further research efforts.

Lee's story inspired people far and wide, even many who never had the chance to meet him. Driven to Cure has received donations



“Andrew’s efforts to raise awareness for this disorder give hope to all patients affected with this rare form of kidney cancer.”

—DR. W. MARSTON LINEHAN



“Andrew was a wonderful young man and an inspiration to our entire clinical team,” said Dr. W. Marston Linehan, chief, Urologic Oncology Branch, NCI. “From the moment he was diagnosed, his thoughts turned to

from 160 countries and plans to continue its charitable work in Lee's memory.

“It has been an honor to have had the opportunity to care for such a brave and selfless individual and to get to know his equally remarkable family,” said Linehan. “Andrew's efforts to raise awareness for this disorder give hope to all patients affected with this rare form of kidney cancer.”

Lee is survived by his parents, Bruce and Sarah, brother Tommy and girlfriend Hailey.—Dana Talesnik



NIDA's Compton Receives HHS Award at Ceremony

Dr. Wilson Compton, deputy director of NIDA, received the Department of Health and Human Services' Secretary's Award for Distinguished Service at the annual award ceremony on May 8. The event was held at the Great Hall of the Hubert Humphrey Bldg. in Washington, D.C. Compton was recognized for his service in helping to build data capacity for research under the auspices of the Office of the Secretary Patient-Centered Outcomes Research Trust Fund portfolio. His award highlighted the workgroups that designed new multiagency projects relevant to the secretary's priorities on opioids.

VOLUNTEERS

Study Needs Healthy Children

NICHD seeks healthy children 7 to 11 years old with above average weight to join in a research study. Researchers want to learn if breaking up sitting with short periods of activity improves children's metabolism and attention. Six outpatient visits on consecutive days of about 3 hours each (Monday-Friday, early evening and Saturday morning) are required. Compensation will be provided. For more information, call 1-866-444-2214 (TTY 1-866-411-1010). Read more at <https://go.usa.gov/xRPAg>. Refer to study 17-CH-0130.

HIV Vaccine Study Needs Subjects

Vaccine Research Center researchers seek persons 18-60 years old who are living with HIV for a research study. The study evaluates an investigational product targeting the HIV virus to determine if it is safe and can generate an immune response. Compensation is provided. For more information, call 1-866-444-1132 (TTY 1-866-411-1010) or email vaccines@nih.gov. Se habla español.

NIH Record

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE May 25, 1959, Vol. XI, No. 11

\$5200 IN AWARDS GIVEN AT PROGRAM HERE

Superior performance awards were given to 60 employees for superior performance and suggestions, and 81 others received length-of-service pins at the annual spring awards ceremony held at the CC Auditorium May 6.

Principal speaker of the ceremony was NEW Under Secretary Bertha S. Adina, who stressed the high rate of adoption of suggestions, and added that the Department anticipates expanding the program.

The comments of Dr. John D. Rockefeller, Director of the Department, were read by NIH Deputy Director C. J. Van Dyke. Increasing the value of continuity of service, Dr. Rockefeller said, is a

PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

DR. BERLINER ELECTED BY ANCIENS' GROUP

Dr. Robert W. Berliner, Associate Director in Charge of Research, NIH, was elected president of the American Society of Clinical Investigation at the annual meeting May 4 in Atlantic City.

Dr. Berliner is the first Government scientist to be elected to such a post in the 50-year life span of the society.

An authority on renal function and electrolyte metabolism, Dr. Berliner has been a member of the NIH staff since 1950, and Research Director since 1954. He was formerly assistant professor of medicine at Columbia University, New York.

DR. DORN CHOSEN CUTTER LECTURER

Dr. Harold F. Dorn, Chief, Biometrics Branch, DHEW, delivered the Cutter Lecture at Harvard University on May 10. His subject was "Some Problems Arising in Prospective and Retrospective Studies of the Etiology of Disease."

Dr. Dorn was appointed Cutter Lecturer on Preventive Medicine for the academic year 1958-59. The lectureship, set up in 1953, was established in the will of Dr. John Clarence Cutter, a graduate of Harvard Medical School. Most of the lectures have concerned

NEW Under Secretary Bertha S. Adina addresses NIH employees during awards ceremony at the CC Auditorium. The "Awards" luncheon was the most popular program.

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the NIH Record

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE May 22, 1961 Vol. XI, No. 10 NATIONAL INSTITUTES OF HEALTH

Conferees Will Describe Progress in Developing Artificial Heart Devices

On Monday, June 5, Dr. Frank B. Rowland, Chief of the Division of Heart and Lung Diseases, will preside at the annual meeting of the American Society of Artificial Heart Devices, Inc., at the Sheraton Hotel, Washington, D.C.

Dr. Rowland is chief of the Division of Heart and Lung Diseases, and is also Chief of the National Heart Institute. He will be joined by Dr. Robert W. Berliner, Associate Director in Charge of Research, NIH, and Dr. Robert C. Byrd, Chief, Division of Heart and Lung Diseases, NIH.

Dr. Conroy Is Appointed BEAT Assc. Director For Program Planning

Dr. Robert A. Conroy has been appointed Associate Director for Program Planning and Evaluation of the Bureau of Health, Professions and Biomedical Services, DHEW.

Dr. Conroy has been a member of the staff of the Bureau of Health, Professions and Biomedical Services since 1954. He was formerly Director of the Division of Biomedical Services, DHEW.

DR. DORN CHOSEN CUTTER LECTURER

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King Boudouin, Queen Fabiola of Belgium Visit NIH, Tour Clinical Center Facilities

The King and Queen of Belgium, accompanied by Dr. Robert C. Byrd, Director of the Division of Heart and Lung Diseases, NIH, and Dr. Robert W. Berliner, Associate Director in Charge of Research, NIH, visited the National Heart Institute on May 10. They were accompanied by Dr. Robert C. Byrd, Director of the Division of Heart and Lung Diseases, NIH, and Dr. Robert W. Berliner, Associate Director in Charge of Research, NIH.

The NIH Record

U.S. Department of Health, Education, and Welfare May 15, 1971, Vol. XXII, No. 10 National Institutes of Health

Carnival Flavor Theme Of Health Weeks '79

Good health is more than a passing fancy and getting vaccinated. Good health depends on the way we live. That's the focus of HEALTH WEEKS '79, to be held May 20-26, 10 a.m. to 5 p.m., on the Mall from NIH Headquarters.

HEALTH WEEKS '79 will include a carnival setting—concerts, exhibits, lectures and demonstrations, plus a parade through the city. The parade will feature floats, stunts, games, singing, and dancing. There will also be a parade of health professionals and their families, and safety and emergency personnel.

Four NIH Researchers Among New Members Elected to National Academy of Sciences

Four NIH scientists were among 40 new members elected to the National Academy of Sciences in recognition of their distinguished and continuing achievement in their respective fields.

The new members are: Dr. Robert W. Berliner, NIH; Dr. Robert C. Byrd, NIH; Dr. Robert A. Conroy, NIH; and Dr. Robert H. Workman, NIH.

Further Research on Transfusion Therapy Stressed at CDC Consensus Conference

Further research should be conducted on the possible effects of transfusion therapy for patients with sickle cell disease, the consensus conference on transfusion therapy for sickle cell disease, held at the CDC on May 10-11, stressed.

The conference was held at the CDC in Washington, D.C. It was attended by experts in the field of transfusion therapy for sickle cell disease.

DR. EARL REECE STADLER ELECTED AAAS FELLOW

Dr. Earl Reece Stadler, Chief, Laboratory of Biophysics, NIH, has been elected a Fellow of the American Association for the Advancement of Science (AAAS).

Dr. Stadler is a member of the AAAS Council and is also a member of the AAAS House of Delegates. He is also a member of the AAAS Board of Directors.

NIH Record issues from three early decades (from l) 1959, 1969 and 1979 show that NIH science may belong to the world, but its people belong to one another.

THE RECORD-ING INDUSTRY

NIH Record Marks 70th Anniversary

When a record goes platinum, that means it has sold at least 1 million copies. Platinum is also what folks, at least in the U.K., use to mark a 70th anniversary.

On May 20, 1949, the *NIH Record* debuted on campus. It has been published continuously since then, a product of the Office of the Director's Office of Communications and Public Liaison.

For 70 years, the newsletter has had the privilege of telling NIH stories about itself, a biweekly snapshot of the progress of medical research at its leading edge.

The best novels, they say, show and do not tell. You can pick a copy of the *Record* from any era (by going to https://nihrec-ord.nih.gov/past_issues.htm) and, in an instant, glean a sense of a vibrant,

NIH Record

FEDERAL BUREAU OF INVESTIGATION 20 May 1949 PUBLIC HEALTH SERVICE NATIONAL INSTITUTES OF HEALTH

NIH TO HELP COMBAT DISEASE IN AFRICA

SOFTBALL AGAIN! BUT WHERE ARE THE DOCS?

When Dr. John Boscicovich yelled "Batter up!" on May 11 to start the first NIH softball game of 1949, spring was officially here.

There weren't as many doctors running around the new diamond near the main entrance as the old field (now obliterated by construction of the Clinical Center), but the season is young yet. Drs. Norman Topping, F. A. Arnold, I. J. Griffiths, and

WYCKOFF IS ELECTED TO NATIONAL ACADEMY

The election of Dr. Ralph W. G. Wyckoff, Chief of the Section on Molecular Biophysics, XBM1, to the National Academy of Sciences is one of the highest honors that can come to a scientist in this country.

At the annual meeting of the academy, 29 American scientists were elected. Membership is limited to 450. The elections which included Dr. Wyckoff brought the total membership within one of the maximum

DR. BRADY TO MAKE SURVEY FOR BRITISH

Assignment of Dr. Frederick J. Brady, Assistant Chief of the Laboratory of Tropical Diseases, to make a preliminary survey of conditions affecting the control of trypanosomiasis and malaria in East and West Africa has been announced by the Economic Cooperation Administration in Washington and London.

With Mr. Harry H. Stage, associate expert of the U. S. Department of Agriculture, Dr. Brady will

Debut issue May 1949

When you get the job of telling NIH about itself, you don't have a choice. The news is almost always good. And so, we hope, is the messenger.

ambitious, collegial, accomplished and proud institution.

There may not be a "wow" in every issue, but there is certainly a "whew"—there's a lot going on here, an extremely talented workforce and a staggering variety of interests, both at work and at leisure.

The many editors and writers from both OD and all of the institutes and centers who have provided *Record* content have made this journey one issue at a time, not with the explicit goal of telling good and hopeful news, even if that is what, in sum, it has amounted to.

The NIH Record

Director Reflects on 7½ Years at NIH

By Rick McManus

For one of a biweekly issue...

NIH's Legislative Father

Bldg. 31 Renamed: Honors Claude Pepper

NIH's Legislative Father

Bldg. 31 Renamed: Honors Claude Pepper

NIH's Legislative Father

Bldg. 31 Renamed: Honors Claude Pepper

NIH Record

New Advisory Group Meets For First Time

COPR Provides New Forum For Interacting with Public

NIH Record Celebrates Its 40th Anniversary

NIH Record Celebrates Its 40th Anniversary

nih record

60th Anniversary Issue

Week-Long Event Builds Excitement

Just Past Infancy, Nanomedicine Takes 1st Steps at NIH

NIH Record Celebrates Its 40th Anniversary

NIH Record Celebrates Its 40th Anniversary

The *Record* has packed a lot of news into the past 30-odd years, as anniversary front pages, above, reflect.