

GAMING MEDICAL RESEARCH AI Workshop Surveys Landscape, Assesses Big Ideas

BY CARLA GARNETT

It's been nearly 160 years since Milton Bradley introduced a "Game of Life" wherein players navigate around a brightly painted board, landing on spaces that dole out good fortune and bad. Although modern editions billed it as a "game of skill and chance," contemporary Life relied more on the whimsy of a Wheel of Fortune than on personal acumen for success. At the Day of Reckoning you were as likely to wind up a millionaire as a pauper. That's life, right?

What if players had extraordinary,

suprahuman help, though, to foresee dangers, dodge misfortunes and seize advantages? And what if the game ultimately was your real life—or specifically, your health?

That was the fascinating salvo keynote speaker Craig Mundie launched at a recent all-day workshop devoted to "Harnessing Artificial Intelligence and Machine Learning to Advance Biomedical Research."

We're seeking prescience about our health, the tech oracle suggested. "How do we structure the problem in such a way that



AI workshop speaker Craig Mundie (l) casts a bold vision of medical research in the machine-learning era, as NIH director Dr. Francis Collins looks on.

the machine can learn the answer and tell it to us, as opposed to the other way around?" he asked. "This is a big difference between whether you're just trying to make the

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Movie projectors are spared; see story on p. 12.

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KNOWLEDGE EQUALS...? NHGRI Alum Studies Reactions to Genomic Information

BY RICH MCMANUS



Dr. Saskia Sanderson

returned to a kind of hero's welcome recently when she explored the psychological impact

On the 15th anniversary of the founding of NHGRI's Social and Behavioral Research Branch (and the 25th anniversary of the institute itself), one of SBRB's first postdoctoral fellows—Dr. Saskia Sanderson, who arrived in 2007—

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Summer Interns Share Their Research at Poster Day

BY ERIC BOCK



Maya Moore of NHGRI

Hundreds of students in summer training programs participated in the annual NIH Summer Research Program Poster Day held in Bldg. 45's conference center on Aug. 9.

The exhibition was the result of a summer's

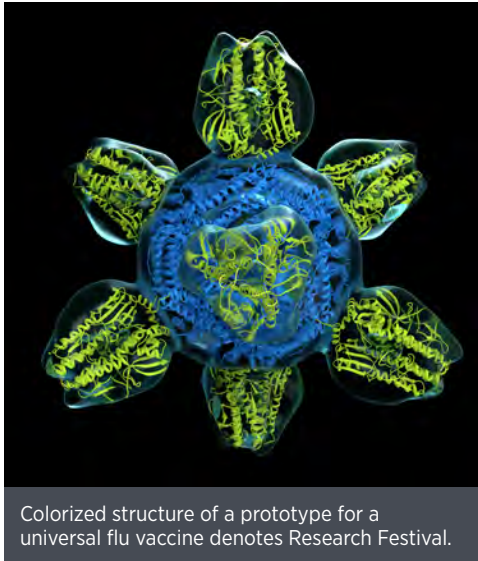
worth of hard work for high school, college, graduate, medical and dental students working in intramural research groups at NIH. The Office of Intramural Training & Education organized the event.

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Research Festival Set, Sept. 12-14

The 2018 NIH Research Festival: A Celebration of Intramural Science will be held Sept. 12-14. The annual festival highlights the diversity of scientific disciplines within the NIH Intramural Research Program.

There will be three plenary sessions, one each morning, on: the research of four IC directors; immunodeficiency and lysosomal disorders; and atopic dermatitis and influenza. The concurrent



Colorized structure of a prototype for a universal flu vaccine denotes Research Festival.

symposia sessions, which will take place in the afternoons, will focus on cell-based gene editing and CRISPR; myeloid malignancies; vascular biology; computational biology, data science and machine learning; high-throughput sequencing; and biochemistry.

The festival will be held in and around Bldg. 10 and will include more than 300 scientific posters. Other highlights include the IC directors and scientific directors poster session; a hackathon; NIH Green Labs Fair and exhibits; the FARE awards ceremony; R&W Taste of Bethesda lunch; animal tribute ceremony; the Technical Sales Association vendor tent show; and virtual reality and technology hub demonstrations at the NIH Library.

Visit <http://researchfestival.nih.gov> for the full schedule and schedule downloading options.

35th Institute Relay Set, Sept. 20

The 35th NIH Institute Challenge Relay will be held on Thursday, Sept. 20 on the south side of Bldg. 10, beginning at 11 a.m. To accommodate the large number of teams, there will be 4 heats this year rather than the usual 2.

The relay consists of teams of five runners, each of whom runs a loop around parking lot 10H. All institutes, centers, divisions and contractors are invited to enter as many teams as they wish. Each team must have men and women, with at least two runners of the same sex.

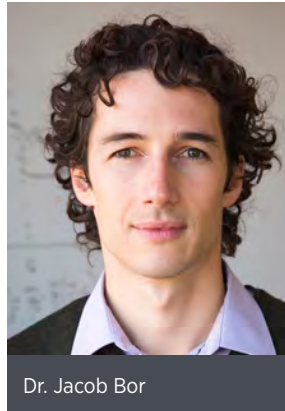
The most important part of the race is to have fun and enjoy the company of your fellow NIH'ers. Register your team for \$25 at www.govemployee.com/nih/event-detail/nih-institute-relay-2018. Each group leader is asked to provide the name and contact info for one volunteer. Make sure to visit with event exhibitors as well. To volunteer or for more information contact David Browne at browned2@mail.nih.gov or (301) 594-2411.

Bor To Give Next 'Mind the Gap' Webinar

Dr. Jacob Bor will give the Office of Disease Prevention's next Mind the Gap webinar about regression discontinuity designs in public health research on Thursday, Sept. 27 at 11 a.m.

Regression discontinuity designs offer an internally valid approach for causal inference without need for randomization. They can be implemented when an exposure is

assigned at least in part based on a threshold rule: the party with more than 50 percent of the votes wins in a two-party election; the HIV patient with a CD4 count below 500 cells is offered therapy; residents downstream of a point pollution source swim in contaminated water. Historically, regression discontinuity designs have been underutilized in public health and medical research. However, the last few years have seen burgeoning use of this method. The presentation will review the theory behind regression discontinuity designs and their implementation, with a focus on examples in public health research.



Dr. Jacob Bor

Bor is assistant professor and Peter T. Paul career development professor in the departments of global health and epidemiology at Boston University School of Public Health. His research applies the analytical tools of economics and data science to the study of population health, with a focus on HIV treatment and prevention in southern Africa. He will accept questions during the webinar via WebEx and Twitter. Use #NIHMTG.

Registration is required and can be done at <https://prevention.nih.gov/education-training/methods-mind-gap/regression-discontinuity-designs-public-health-research>.

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Workshop on Preventing Osteoporotic Fracture, Oct. 30-31

NIH will hold a Pathways to Prevention Workshop: Appropriate Use of Drug Therapies for Osteoporotic Fracture Prevention on Oct. 30-31 at Natcher Conference Center.

More than 10 million people in the United States

have osteoporosis, a skeletal disorder that causes bones to become weak and fragile as a result of low bone mass. The condition makes people more susceptible to fractures, which can impair their ability to live independently and even threaten their lives. Lifestyle changes and medications can help reduce a person's risk of osteoporotic fractures. Bisphosphonates, a first-line pharmacological treatment for most people with osteoporosis, have been found effective with short-term use among individuals who have a high risk of fracture; however, the benefits and risks of longer-term treatment are less clear.

The workshop's goal is to better understand current knowledge gaps and to identify future research needs in using osteoporosis drugs.

For more information and to register visit <http://bit.ly/P2PFracture>.

Lecture on Health Effects of Contact with Nature, Sept. 19

Dr. Gregory Bratman, an environmental scientist at the University of Washington, will speak on "Nature Contact and Human Health: A Multimethod Approach" on Wednesday, Sept. 19 at 11 a.m. in the lecture hall of Bldg. 60. His talk is part of NCCIH's Integrative Medicine Research Lecture Series.

A leader in an emerging field, Bratman's work takes place at the nexus of psychology, public health and ecology. People around the world are increasingly disconnected from nature, as they spend more and more time (in some cases, over 90 percent) indoors. Yet contact with nature has been shown to benefit human beings in a variety of ways.

Bratman will discuss the current state of the

science on nature and mental health, as well as a proposed agenda for future research. He will describe various approaches to measuring the impacts of nature experience on mood, cognitive function and emotion regulation; evidence on the causal mechanisms that may be responsible; and implications for urban planning and public policy.



Dr. Gregory Bratman

The inaugural holder of the Doug Walker endowed faculty fellowship, Bratman is an assistant professor in UW's School of Environmental Science and Forest Sciences. He holds a Ph.D. in environment and resources from Stanford University, where he was a Kelso fellow and a Packard Foundation fellow. The lecture will be streamed on NIH Videocast and Facebook Live, with more information available at <https://nccih.nih.gov/news/events/IMlectures>.

Military a 'Perfect Lab' for Studying Pain, Larson Says

BY ELLEN O'DONNELL

As surprising as it may be, given the size and complexity of the system, health care in the U.S. military has been a true innovator over the past decade in caring for chronic pain and the health problems often associated with it—such as trauma, mood disorders, substance use disorders and sleep problems.

So says Dr. Mary Jo Larson, a senior scientist at Brandeis University's Institute for Behavioral Health and an NCCIH grantee, who lectured recently in Lipsett Amphitheater as part of NCCIH's Integrative Medicine Research Lecture Series. Her focus was nondrug therapies for chronic pain in the Military Health System, which is part of the Department of Defense and delivers health care to 9.4 million beneficiaries worldwide.

Larson described a watershed moment in 2010 when the report of the Army pain management task force was released. The group was chartered by the Army surgeon general to make recommendations for a comprehensive pain-management strategy that would be "holistic, multidisciplinary and multimodal in its approach, utilize state-of-the-art/science modalities and technologies and provide optimal quality of life for soldiers and other patients with acute and chronic pain." It would seek to address problems of deficiencies and unwarranted variability in pain care across DoD, as well as concerns with medication abuse and rising suicide rates that often appeared pain-related. The resulting report contained 109 recommendations under 4 major areas, e.g., "synchronizing a culture of pain awareness, education and proactive intervention."

In the near-decade since, Larson said, innovations in the Military Health System have included 157 primary care medical homes that can provide patient education on self-management of pain, especially musculoskeletal. Almost 200 behavioral health teams have been embedded within battalions and brigades, with the intent of starting mental-health discussions in a non-stigmatized way. Eight flagship interdisciplinary pain-management centers offer specialized care and conduct research (some also train other providers).



The military is an innovator in treatment of chronic pain, says Dr. Mary Jo Larson of Brandeis University.

PHOTO: CHIA-CHI CHARLIE CHANG

Near NIH, the Uniformed Services University is home to the Defense and Veterans Center for Integrative Pain Management. Among its innovations is a free, downloadable defense and veterans pain rating scale that is research-based and validated and measures functional status, not simply pain level.

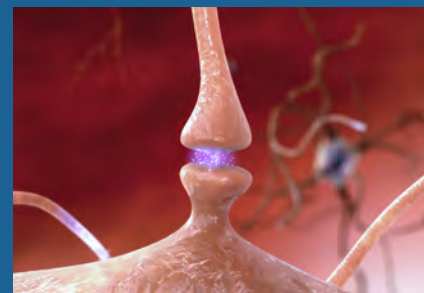
On the research side, "military populations and the Military Health System provide a perfect laboratory for research on how to improve the delivery of care for most U.S. patients with acute and chronic pain," Larson said. "Essentially, you have a young, healthy population, broadly representative of the U.S. population and receiving uniform health benefits, who experience multiple risk factors and are constantly pushing their physical limits. We see the emergence of acute events leading to pain and can watch it develop. It is even more intriguing as neuroscience is learning more about the overlapping brain circuitry involved in chronic pain, PTSD and addiction."

In her NCCIH-funded study, Larson and her team have been building a large collection of data from multiple military health-care databases on all Army soldiers who returned from deployment to Iraq or Afghanistan from 2009 to 2014 (numbering almost 1 million). Using these data, they conduct population-based observational studies, focusing on military-relevant outcomes associated with integrative care modalities.

"Researching which services are delivered, to whom, and when, and how they are organized, is valuable in identifying where to optimize the delivery of pain care," she said. So far, she has identified "opportunities for early delivery of integrative, multimodal care [as we saw in our study of low-back pain] to avert maintenance on opioid medications and potentially to maintain function."

Policy discussions on opioids, Larson said, "have focused almost exclusively on prescriptions and pain levels. We need to spend much more attention on how to restore patients to optimal functioning and helping them live with chronic pain that may not be eliminated. This leads to discussions of reasonable expectations about pain control, and of self-management, self-care and nondrug strategies."

The lecture is available at <https://videocast.nih.gov/Summary.asp?Live=27891&bhcp=1>. **R**



ON THE COVER: *Synapse illustration. In the nervous system, a synapse is a structure that permits a neuron (nerve cell) to pass an electrical or chemical signal to another neuron. Alzheimer's disease disrupts communication among neurons, resulting in loss of function and cell death.*

IMAGE: NATIONAL INSTITUTE ON AGING

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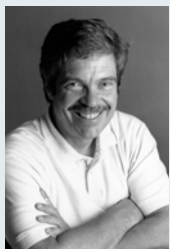
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Kay To Deliver Lindberg-King Lecture, Sept. 26

Computer science pioneer Dr. Alan Curtis Kay will deliver this year's Lindberg-King Lecture on Wednesday, Sept. 26 from 2 to 3 p.m. in Lister Hill Auditorium, Bldg. 38A. His talk is titled "The Best Way to Predict the Future Is to Create It. But Is It Already Too Late?" A child prodigy, Kay was an original member of the seminal Xerox-PARC group, and for his myriad innovations in computer science was awarded the field's highest honor, the Turing Prize. He has been elected a fellow of the American Academy of Arts and Sciences, the National Academy of Engineering and the Royal Society of Arts. He is president of the Viewpoints Research Institute and an adjunct professor of computer science at the University of California, Los Angeles. The Lindberg-King Lecture honors former NLM director Dr. Donald Lindberg and former NLM deputy director of research and education Dr. Donald West King. The event is co-sponsored by NLM, Friends of the National Library of Medicine and the American Medical Informatics Association. The event will also be videocast and archived at <https://videocast.nih.gov/>.



Sanderson

CONTINUED FROM PAGE 1

of learning one's personal genetic information during a talk in Lipsett Amphitheater.

It wasn't like World Cup cheering in a soccer stadium, but it was a bit more boisterous than the usual welcome accorded speakers giving rounds. It was a homecoming after all, acknowledging the success of an alumnus—Sanderson has since gone on to research positions in Manhattan and, currently, in London.

A senior research associate at University College London, Sanderson discussed the utility of genome sequencing for physical and mental health—the balance of benefits versus risks that people compute internally when they stand to know more about their likelihood of disease than they would have had the human genome never been sequenced.

She described a patient, Paul, an otherwise healthy British double-bassist who smoked 20 cigarettes a day and suffered a heart attack at age 37. Would he have changed his behavior had he known his genetic risk of cardiovascular disease, Sanderson wondered?

Paul turned out to be Sanderson's father, still alive, fortunately, and happy to be able to cavort with Sanderson's young son.

With "tens of millions of people" expected to have their genomes sequenced in coming decades—there are already an estimated 25 million people worldwide participating in genome cohort studies—it is important to study the impact this new knowledge will have on individuals' health and behavior, Sanderson believes.

She reviewed a number of studies undertaken in the past decade suggesting that when single genes are examined—such as GSTM1 as a marker for increased risk of lung and esophageal cancer—and a person's risk is found to be relatively low, there is little impact on behavior.

"That's a finding that has really permeated our field," Sanderson said, "that testing doesn't impact behavior." It may, however, prompt initiation of medication and future screening.

After her NHGRI postdoc, Sanderson moved to Icahn School of Medicine at Mt. Sinai in New York City. She and her

★ ★ ★

"At the end of the study, most people wanted a hard drive with their raw data, but no one knew what to do with it."

—DR. SASKIA SANDERSON

★ ★ ★

colleagues studied biobank enrollees' attitudes toward taking part in genomic studies and eventually developed an online education tool to explain whole-genome sequencing to the public.

"We wanted to help people make decisions if they were invited to participate in genomic research."

Another project called HealthSeq examined the utility of participating in genomic studies for people who were in good health. Thirty-five people had their genomes sequenced.

"At the end of the study, most people wanted a hard drive with their raw data, but no one knew what to do with it," Sanderson reported.

Her studies have revealed some interesting dimensions of research participation:

- Scientists want to include diverse populations for robust results, but people in Harlem, just north of Mt. Sinai, proved too under-insured to enroll; they could not afford the care they might need if something negative turned up.

- Simple curiosity and concern about risk of disease motivate most people to participate in genetic studies.

- As polygenic, rather than single-gene, risk scores become available, based on millions of common DNA variants, it will become even more important to evaluate the benefits vs. harms of such testing.

"We hope to be able to identify early those at risk of developing mental health problems," Sanderson noted, "but the harm is the stigma involved...How do we maximize the benefits and minimize the harms?...We need to do this right, if we're going to do it."

During a brief Q&A session, Sanderson concluded, "None of this information is deterministic—it's all about risk...People have a hard time with risk. They want hard answers, yes or no. Communication is a big issue. We have to work out how to talk to people about this. It's an uncertain field."

The talk was part of the NHGRI intramural program's silver anniversary summer seminars, given by successful NHGRI trainees.



"People have a hard time with risk. They want hard answers—yes or no. Communication is a big issue," said Sanderson. "We have to work out how to talk to people about this. It's an uncertain field."

PHOTOS: LISA HELFERT



Sam Caldwell insists on a winning attitude as a leader's key attribute.

Training Is Key to Building Winning Culture

BY ERIC BOCK

To create a winning culture, supervisors must communicate expectations, motivate others to do their jobs and believe their employees can succeed, said Sam Caldwell at the “Training for Success” NIH Employee Training Conference held recently in Bldg. 45.

“Unfortunately, most people don’t appreciate good leadership until they start experiencing bad leadership,” said Caldwell, athletic director and varsity girls basketball coach at New Hope Academy in Landover Hills, Md.

In 2005, he was hired to be head coach for the All-Navy basketball team. All-Navy teams are part of the Department of Defense’s sports program. Players compete in the Armed Forces sports championships against teams from the Marine Corps, Army, Air Force and Coast Guard.

The Navy team hadn’t won a championship since 1990, so Caldwell was under pressure to succeed right away. His supervisors thought his background as a former player positioned him for success.

Before he was hired, previous coaches would select 12 players on the basis of their applications. Caldwell knew he couldn’t identify winning players by reading about

their qualifications. He held 5 regional, 2-day mini-camps so he could observe players’ work ethic, attitude and body language.

After the mini-camps, he invited 30 players to participate in a training camp. He then selected 12 players to be part of the team. From the previous year’s squad, he cut all but one player.

He hired an assistant coach with experience coaching in DoD’s sports program. The coach asked what Caldwell’s goal for the year was. He replied, “My goal for this year is to win a championship.” The coach began laughing so hard he almost fell out of his chair. He thought Caldwell didn’t select experienced players.

Caldwell fired him on the spot because the assistant believed the team couldn’t win. If coaches don’t believe they can win, players won’t believe they can win, either.

“He couldn’t see that I wasn’t looking for playing experience. I was looking for attributes of winners—guys who had an opportunity to win something before, who would do anything to play at this level or who suffered an injury and were coming back and wanting an opportunity to play and compete at a high level,” Caldwell said.

He demanded a lot from his best players. He reasoned that if the best players put in the most effort, the other players would follow. That’s exactly what happened. The team, for

example, began to show up to practice earlier than their coach. They went on to win the championship by 20 points.

In his current position as varsity girls’ basketball coach, Caldwell tells his players that “no one is going to work harder or have more fun than us.” He doesn’t hide that he wants to be the best. “Somebody has to be number one. Might as well be me,” he said.

He believes success is a process that can be repeated. “That’s why you can take a CEO and they can go anywhere and build an organization

from the ground up. They can go and make a place better because they know what winning looks like,” he added.

The conference was hosted by the trans-NIH training conference committee. Attendees learned best practices and next practices in training activities and initiatives. The event also included a plenary session, breakout sessions and an exhibition of NIH training groups.



Participating in a panel discussion on best practices are (from l) Elena Juris, director of the NIH Training Center; Susan Silk, director of the NIH Office of Laboratory Animal Welfare’s Division of Policy and Education; Dr. Craig Giroux, scientific officer training specialist at the Center for Scientific Review; and moderator Kristen Dunn-Thomason, NIH chief learning officer and director of the Office of Human Resource’s Workforce Support and Development Division.

PHOTOS: CHIA-CHI CHARLIE CHANG



Mundie (l) suggests the computer gaming world has important lessons for medical research. At right, Collins talks about mining homogenous data sets such as the Human Genome Project.

PHOTOS: CHIA-CHI CHARLIE CHANG

AI

CONTINUED FROM PAGE 1

machine do what you already know how to do—things it can do more efficiently—or, are you saying, ‘No, the machine can know things I’ll never find out?’ That’s a very different way to think.”

Held appropriately in NIH’s on-campus brain center, the Porter Neuroscience Research Center, the meeting gathered thousands of in-person and online attendees—both the AI-experienced and the AI-curious—to explore what NIH director Dr. Francis Collins called “something pretty profound.”

Artificial intelligence, “considered to be the bigger umbrella, can sense, reason, act and adapt,” he said, defining terms at the outset. Machine learning (ML) refers to algorithms “whose performance improves as they are exposed to more data over time, with the learning aspect being the emphasis.”

Collins sought advice on how NIH should engage AI and ML to manage the huge amounts of data the biomedical field is generating and collecting and aim that knowledge toward improving health.

AI, big data, robotics and cloud computing are all included in what some have categorized as “the fourth industrial revolution,” he said, putting the workshop in historical context. “This topic is certainly one that is due for a deep dive by NIH leadership in terms of where we are and where we might need to go.”

The goals of the workshop were to survey

the state of AI for biomedical research, dig deeper into specific examples, explore opportunities for NIH to make maximum impact and identify key challenges and obstacles and how can NIH help solve them.

The event also featured numerous innovative ideas presented during two plenary sessions (see sidebar) and discussions afterwards with audience and speakers.

Ultimate Chess Match

Stirring the pot first, though, was former “visionary-in-residence” at Microsoft Mundie with a provocative proposition:

AI Applied in Clinical Settings

In addition to a disruptive keynote talk by tech thought leader Craig Mundie, the recent all-day artificial intelligence (AI) workshop heard a number of practical considerations and applications of machine learning in clinical settings that provided NIH with plenty of food for thought.

Dr. Dina Katabi of MIT’s Center for Wireless Networks and Mobile Computing introduced the “health-aware home,” her lab’s AI clinical application prototype.

Using the electromagnetic field surrounding everything, the group’s wi-fi-like technology can track and measure people’s breathing, sleep, heart rate, falls and gait speed—all without attaching sensors to the subject. The device transmits low-level wireless signals and uses AI to analyze the signals. It’s already been tested in assisted-living facilities with people who are elderly or who have sleep and breathing disorders, Parkinson’s disease or other chronic health problems.

“The future in health care is terrific,” Katabi said,

AI learns faster and better than humans ever will, so why not give it all of the raw biological data and let the machine learn the pathways and functioning of human biology and use that to predict or find ways to resolve high-dimensional problems such as complex disease?

The longtime tech mega-consultant is known for identifying patterns in information, matching compatible designs and concepts and foreseeing how they could possibly work together to transform whole industries. In the past few years, he’s directed this talent toward the health and biomedical research fields.

Collins invited Mundie to envision NIH’s ideal role regarding the artificial intelligence age; for inspiration, Mundie looked to the computer gaming world. He began by asking a bold question: “Is human biology too complicated for humans to figure out?”

Remarkably in this age of “big data,” he wasn’t endorsing putting more resources into mining gigantic data sets. Mundie’s prescriptions leaned more toward “minimization as opposed to maximization.” So, he posited, we have the human genome and the proteome and maybe that’s as many “omes” as we need to feed into the machines.

“Most of everything we’ve done in data-driven biology and medicine starts with the assumption that we look at a population and try to extract from that population things

“and computer science with additional technology, AI and machine learning will come together to provide much stronger types of data and also provide information for the health care system to improve the quality of care.

“Imagine what would happen if we had a device like this in the home of every chronic disease patient—how much more we would learn about diseases, how much more we would be able to intervene before exacerbation. I think we can do that if we start thinking together, bringing the computer scientists, people who work on AI, with people who are in the health care system—the doctors, the biologists, the bioengineers, the chemists—and creating that future.”

NIH’s own Dr. Ronald Summers of the Clinical Center offered proof that machine learning can significantly improve precision and accuracy in biomarker imaging diagnostics.

Dr. Judith Dexheimer of Cincinnati Children’s Hospital talked about her group’s research on making the wealth of data contained in electronic health records, or EHRs, more universally useful and accessible.

that we then apply to the individual,” he said. “My prediction is that the future of medicine is all about starting with the individual, and ultimately, as you see enough commonality, you’ll synthesize the population answer—that’s completely upside down from everything the world currently has done.”

Humans, No Monopoly on Knowledge

Mundie’s “penicillin discovery moment” occurred as he encountered recent reports from the computer gaming community. Professional machine-learning gamers studying how AI could be applied to the

games in a matter of days—more than any human player could hope to experience in a lifetime.

Then, Mundie observed a chance situation in biology where the learning system compensated for a human error in providing requisite data and got a better answer without it.

“These things learn at a scale that humans cannot do and never will be able to do,” he explained.

Showing an article from the most recent *Harvard Business Review*, Mundie said, “They like many others are wrestling with



“We want our approach to AI to be more than just ‘A.’ The ‘artificial’ part comes really easily, but we need lots of ‘I,’ the intelligence part—and better yet, we need both of those together.”

—NIH DIRECTOR DR. FRANCIS COLLINS



ancient game “Go” or to solving Rubik’s Cube were coming to terms with their human frailties—computers were increasingly employing the sheer scale of their AI advantage to beat human experts every time. The machines were synthesizing and learning from the different maneuvers and strategies of millions of iterations of the

the question of “What does it mean for mankind when the computer does all of the things that we do?” They suggest a collaboration between human and machine where the humans provide three key capabilities—training, explaining and sustaining. He questioned whether the first two were really required.

Other action items he noted include the need to prioritize, harmonize and clean up data sets and better enforce provisions giving researchers access to such data; plan for quantum computing; and build a broader community for people in AI-related professions exploring health research applications.

Collins also said he intends to bulk up NIH’s brain trust, “deepening our own bench.” He’ll follow up the AI conference by convening a working group within his advisory committee to the director.

“We have a critical opportunity here now and we don’t want this moment to come up and go down without having some legs,” he concluded. “What exactly those legs should look like will have to involve some folks who can think big and give us big advice...”

“We want our approach to AI to be more than just ‘A,’” Collins concluded. “The ‘artificial’ part comes really easily, but we need lots of ‘I,’ the intelligence part—and better yet, we need both of those together. And we’re only going to get there if you help us.”

Clue to Health?

Perhaps the biomedical research community—and NIH in particular—should get into the game-design business, Mundie said, sketching an outline of the potential competition.

“Life is just a tournament of multi-player games,” he said. “To win this game, teams have to get the most people to have the longest, highest quality existence. Every game is unique.”


Who are the players? “Mother Nature is a player and she has two tools—randomness and evolution,” Mundie said.

Other contenders are the environment, which includes the physical world as well as political, financial, policy, governance and computing infrastructure factors. Of course, AI and ML—“the bots”—are playing the game too. Their role is to help humans, who include individuals and the people employed in the medical research, health care delivery and wellness and prevention ecosystems.

“This is really an interesting way to think about applying all the different elements of AI to this problem,” Mundie concluded. “This approach discards existing history about biology and medicine and builds an understanding of pathways and interventions up from the individual rather than down from the population. Ultimately, humans will trust—rather than understand—what the machines know and do, just as they do with most of the computerized infrastructure in their lives.”

And how would success be measured? Many in the audience wanted to know.

“What I consider to be winning for me personally, I’d like to live my life where my physical body and my mental capacity stay in sync and in the end they kind of get extinguished together,” Mundie concluded.

The entire workshop is archived at <https://videocast.nih.gov/summary.asp?Live=28053&bhcp=1>. 



Dr. Dina Katabi of MIT discusses AI innovations in clinical research and clinical care.

The event’s line-up also included intriguing talks by Eileen Koski of Microsoft, Dr. David Heckerman of Amazon and Dr. Anshul Kundaje of Stanford.

It’s clear that “we need to rather quickly escalate our involvement and our investment,” said NIH director Dr. Francis Collins, offering closing thoughts at day’s end.

Poster Day

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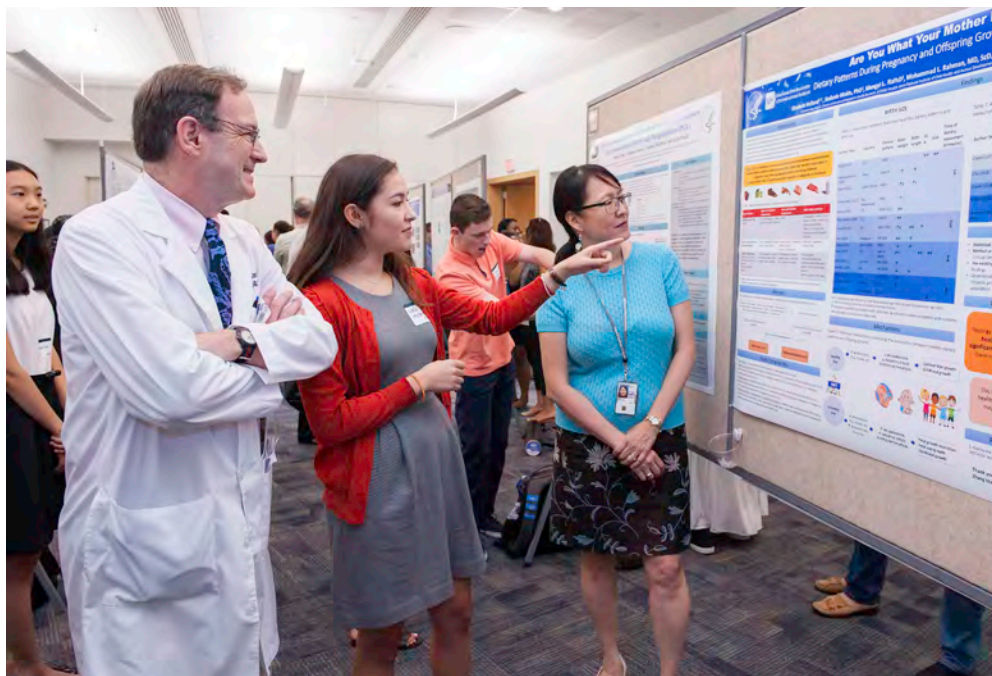
“There was a tremendous amount of positive energy. Students were excited to share what they did,” said OITE director Dr. Sharon Milgram. “The NIH scientists who came were engaged with the interns and the large amount of family members, teachers and supporters from outside NIH added a specialness to the day.”

More than 1,000 students presented during 4 2-hour sessions throughout the event. They explained their research to their peers and other members of the NIH community.

One of the presenters was Calandra Whitted, a doctoral student at Florida A&M University. She took part in the Graduate Summer Opportunity to Advance Research (G-SOAR) Program that started as a partnership between OITE and the chief officer for scientific workforce diversity.

Whitted interned with NHGRI. She helped develop a family health education program to support collecting and sharing family health history in African-American communities. The program will be piloted at Georgetown University’s Lombardi Comprehensive Cancer Center this fall. If all goes according to plan, she will then use the program in rural Florida.

The final session of the day featured students enrolled in the High School Scientific Training and Enrichment Program. Its goal is to expand the pipeline of students interested in biomedical and health care careers by providing opportunities for high school students from schools with a large population of financially disadvantaged students.



Husband and wife Dr. Steven Holland of NIAID and Dr. Maryland Pao of NIMH listen to their daughter, NICHD’s Elizabeth Holland, present her poster.

Participants were encouraged to present even if they didn’t have final results. The purpose of poster day, explained Milgram, is to develop writing, problem-solving and oral communication skills.

“Scientists do research and then they communicate about it when it’s successful and when it’s not as successful,” she said. “We want students to begin developing those skills at the beginning of their careers.”



Clockwise, from above: OITE director Dr. Sharon Milgram (c) helps out at the registration table. A visitor experiences a zebrafish brain in 3-D; NICHD’s Chris Hurt helped create the virtual reality feature described in his project, “A Zebrafish Brain Atlas in a Lightweight Web Browser Environment.” Interns explain their research to their peers. More than 1,000 students presented posters in the Natcher Bldg. conference area.

PHOTOS: MARLEEN VAN DEN NESTE



Researchers Identify Key Brain Circuits for Reward-Seeking, Avoidance Behavior

Researchers have identified connections between neurons in brain systems associated with reward, stress and emotion. Conducted in mice, the new study may help untangle multiple psychiatric conditions, including alcohol use disorder, anxiety disorders, insomnia and depression in humans.

“Understanding these intricate brain systems will be critical for developing diagnostic and therapeutic tools for a broad array of conditions,” said Dr. George Koob, director of the National Institute on Alcohol Abuse and Alcoholism, which contributed funding for the study. NIMH also provided major support for the research.

A report of the study, by first author Dr. William Giardino and colleagues at Stanford University, appeared in the August 2018 issue of *Nature Neuroscience*.

Responding appropriately to aversive or rewarding stimuli is essential for survival. This requires fine-tuned regulation of brain systems that enable rapid responses to changes in the environment, such as those involved in sleep, wakefulness, stress and reward-seeking. These same brain systems are often dysregulated in addiction and other psychiatric conditions.

In the new study, researchers looked at the extended amygdala, a brain region involved in fear, arousal and emotional processing and which plays a significant role in drug and alcohol addiction. They focused on a part of this structure known as the bed nucleus of stria terminalis (BNST), which connects the extended amygdala to the hypothalamus, a brain region that regulates sleep, appetite and body temperature.

The hypothalamus is also thought to promote both negative and positive emotional states. A better understanding of how the BNST and hypothalamus work to coordinate emotion-related behavior could shed light on the emotional processes dysregulated in addiction.

That Stinks! 1 in 15 Americans Smell Odors That Aren't There

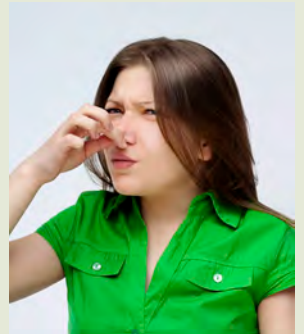
Imagine the foul smell of an ash tray or burning hair. Now imagine if these kinds of smells were present in your life, but without a source. A new study finds that 1 in 15 Americans (or 6.5 percent) over the age of 40 experiences phantom odors. The study, published in *JAMA Otolaryngology-Head and Neck Surgery*, is the first in the U.S. to use nationally representative data to examine the prevalence of and risk factors for phantom odor perception. The study could inform future research aiming to unlock the mysteries of phantom odors.

The study was led by Dr. Kathleen Bainbridge of the Epidemiology and Biostatistics Program at NIDCD. She and her team used data from 7,417 participants over 40 years of age from the 2011-2014 National Health and Nutrition Examination Survey (NHANES). The NHANES data were collected by the National Center for Health Statistics, which is part of the Centers for Disease Control and Prevention; data collection was partly funded by NIDCD.

“Problems with the sense of smell are often overlooked, despite their importance. They can have a big impact on appetite, food preferences and the ability to smell danger signals such as fire, gas leaks and spoiled food,” said Dr. Judith A. Cooper, acting NIDCD director.

Dr. Donald Leopold, one of the study’s authors and clinical professor in the department of surgery at the University of Vermont Medical Center, adds that patients who perceive strong phantom odors often have a miserable quality of life and sometimes cannot maintain a healthy weight.

The ability to identify odors in the environment is known to decrease with age. This study found that the prevalence of phantom odor perception also decreases with age and, interestingly, is not related to individuals’ ability to correctly identify odors.



Researchers Find Potential New Gene Therapy for Blinding Disease

Scientists funded by the National Eye Institute report a novel gene therapy that halts vision loss in a canine model of a blinding condition called autosomal dominant retinitis pigmentosa (adRP). The strategy could one day be used to slow or prevent vision loss in people with the disease.



“We’ve developed and shown proof-of-concept for a gene therapy for one of the most common forms of retinitis pigmentosa,” said Dr. William Beltran of the University of Pennsylvania School of Veterinary Medicine, a lead author of the study, which appeared online Aug. 20 in the *Proceedings of the National Academy of Sciences*.

Retinitis pigmentosa refers to a group of rare genetic disorders that damage light-sensing cells in the retina known as photoreceptors. Rod photoreceptor cells enable vision in low light and require a protein called rhodopsin for their light-sensing ability. People with adRP caused by mutations in the rhodopsin gene usually have one good copy of the gene and a second, mutated copy that codes for an abnormal rhodopsin protein. The abnormal rhodopsin is often toxic, slowly killing the rod cells. As the photoreceptors die, vision deteriorates over years or decades. Scientists have identified more than 150 rhodopsin mutations that cause adRP, challenging efforts to develop effective therapies.

The research team generated a gene therapy construct that knocks down the rod cells’ ability to produce rhodopsin using a technology known as shRNA (short-hairpin RNA) interference.

Gene therapy introduces genetic material, like shRNA, into cells to compensate for abnormal genes or to make a beneficial protein. Often adapted from viruses, vectors are engineered to effectively deliver this genetic material into cells without causing disease.

“The beauty of this novel gene therapy product is in its elegant vector design. I hope it works as well in humans, too,” said Dr. Neeraj Agarwal, translational research program director at NEI.

Pavlidis Retires After 53-Year NIH Career

BY ERIC BOCK

On Aug. 31, John Pavlidis retired as senior structural engineer in the Technical Support Branch of the Office of Research Facilities' Division of Technical Resources. He had worked at NIH since 1965.

"I have greatly enjoyed my engineering career at NIH," said Pavlidis. "The work is challenging, the leadership outstanding. My coworkers are a joy to work with."

Pavlidis reviewed construction projects at intramural research facilities on the main campus, Research Triangle Park, N.C., and Rocky Mountain Laboratories in Hamilton, Mont. Since 2006, his Excel log indicates he interacted on/reviewed more than 5,800 projects.

The Washington, D.C., native graduated from the University of Maryland in 1957. Soon after, he was commissioned ensign in the U.S. Navy's Civil Engineering Corps. While in the Navy, Pavlidis administered construction projects in Charleston, S.C., and on an island 300 miles off the coast of Brazil.

After an honorable discharge, he took a position at John G. Loehler and Associates, an architecture/engineering firm located in Kensington. In that position, he designed levels of the central tower and flying buttresses for the Washington National Cathedral.



Engineer John Pavlidis

Then he learned that NIH was recruiting and applied and got a job in 1965 as a structural engineer. A year later, Pavlidis headed the Engineering Design Branch's development, estimating and specifications section. In that role, he directed research for flooring and wall finish materials for animal facilities and set NIH standards for metal partitions and for laboratory shelving.

In 1998, he was part of a group that received the NIH Director's Award for development of national guidelines for biomedical lab facilities. The guidelines have evolved into national and international standards.

On Aug. 23, 2011, a rare earthquake shook NIH's campus. Pavlidis consulted with his colleagues immediately after feeling the tremors. He first went to the parking garage beneath the Clinical Center

to inspect columns for damage. Inspections continued across campus for garages and buildings. Luckily, all buildings remained structurally sound.

Pavlidis recalls that he met then-NIH director Dr. Bernadine Healy at her departure reception to thank employees. He told her, "It's good we have never met." When she asked why, he responded, "I am a structural engineer."

"NIH is a friendly place to be," Pavlidis concluded. "I have a lot of respect for all our people, and appreciate that they informed us, for review, about any item that appeared to them to be a structural safety issue."

In retirement, he plans to move to Williamsburg, Va., with his wife of 56 years, Connie, who was a Public Health Service officer in the Clinical Center's nursing department.



Juli Egebrecht

NIH CPR Instructor Egebrecht Ends 33-Year Career

BY DANA TALESNIK

During her 33 years at NIH, Juli Egebrecht has touched the hearts of thousands of smart people, and quite a few dummies too. A teacher of CPR (cardiopulmonary resuscitation) and AED (automated external defibrillator) use to NIH employees since 1985, she will retire this month.

"I've met so many wonderful people by doing this work," said Egebrecht, director of basic life support training at NIH. "I see them out and about and some will say to me, 'You look so familiar!' I just have to say '...and 1 and 2 and 3' and it's a lightbulb moment."

Anyone with a medical license of any kind—doctors, therapists, nurses, other health care providers—must have active CPR certification. In the early days, Egebrecht recounted, CPR class lasted all day and clinicians were required to take half-day recertification classes annually. "So I really

Senator, Congressman Visit NIH

On July 30, NIH hosted separate visits by Sen. Tom Udall (D-NM) and Rep. Ro Khanna (D-CA), both of whom met first with NIH leadership before pursuing personal interests. Udall was principally interested in studies of the human microbiome and visited the NIDDK Liver Diseases Branch in Bldg. 10. Khanna discussed the potential of NIH partnerships with Silicon Valley big-data companies and learned about food allergy research. In the photo at right, Udall (third from l) and his assistant Lauren Arias-Jones get oriented to the Clinical Center by NIH principal deputy director Dr. Lawrence Tabak (l) and NIH director Dr. Francis Collins (r). Below, Khanna (second from r) meets with (from l) Tabak; Dr. Daniel Rotrosen, director of NIAID's Division of Allergy, Immunology and Transplantation; NIAID director Dr. Anthony Fauci; Dr. Robert Wood, director of pediatric allergy and immunology at Johns Hopkins University School of Medicine; and Will McKelvey, Khanna's legislative assistant.

PHOTOS: MARLEEN VAN DEN NESTE



got to know the people here," she said. Now, all CPR classes last a half day and renewal is required every 2 years.

"I'm a realist. I know why people are here—they have to be here," said Egebrecht. "But when you think about it, most sudden cardiac arrests occur at home. It may not be your home; it may be a neighbor's home...And people may call upon you while they're waiting for the rescue squad to come. Part of my training is to prepare you for those instances as well as working as part of the [medical] co-team."

It's hard to know how many lives Egebrecht's instruction has helped save over the years, but one story stands out in her mind. An NIH doctor administered CPR on a child who nearly drowned at the resort where he was vacationing. The doctor had just taken Egebrecht's class a few days earlier.

The best part of her job? "It's the possibility of saving someone's life, when it comes right down to it."

Originally from Wisconsin, Egebrecht moved to the Washington area in 1969, the same summer, she noted, that football coach Vince Lombardi left Green Bay for Washington, turning her into a dual Packers and Redskins fan.

Egebrecht started teaching Wednesday night CPR classes at the YMCA in Silver Spring before coming to NIH, where she worked part time on a per diem. This schedule allowed her to stay at home part-time with her daughters, Ronni and Julia. She would later transition to NIH full time.

Egebrecht was grateful to NIH for allowing her to take extended leave in 1996 to fulfill a dream opportunity, serving as an equestrian event judge at the Olympics in Atlanta. She always loved

horseback riding and had previous horse trials experience as a jump judge at the local, state and national levels.

Another of Egebrecht's long-time interests is international travel. Some of her trips to Europe were to visit exchange students her family hosted over the years.

"Knowing those kids and being here at NIH, seeing folks from all over the world come through class, it really expanded the world for me," she said. "Everybody here is your family and it's fun meeting branches of the family you didn't know existed."

Egebrecht has been busy going through mounds of stuff accumulated from decades of living in the same house with her husband, Ron, who died of cancer 2 years ago. Once retired, she plans to sell the house and move, with her dog Ben, back to the family's house in Wisconsin. The home, which has been in her family for generations and is used by extended family as a retreat for holidays and vacations, backs onto a spring-fed glacial lake. She also looks forward to getting back to Lambeau Field for some Packers games.

Her children are grown, and she smiled recollecting how her granddaughter Amanda, 20, has visited her at work since she was a baby, coming with her mom, Ronni, who sometimes helped clean the mannequins. Egebrecht proudly gave Amanda her first CPR training card at the age of 10.

Reflecting on her career, Egebrecht is grateful to have spent a lifetime doing work she loved.

"We are one whole human family, and anything we can do to help folks survive, even something as common as a heart attack that goes into cardiac arrest, is something that adds to keeping your family intact."



Dr. Elliot Vesell

Alumnus Vesell Mourned

Dr. Elliot Vesell, who served as a clinical associate at what was then the National Institute of Arthritis and Metabolic Diseases from 1963 to 1965, and who was head of the section on pharmacogenetics at the National Heart Institute from 1965 to 1968, died on July 23.

A native of New York City, he attended Harvard College, where he majored in American literature and history and graduated both *magna cum laude* and Phi Beta Kappa. He then went to Harvard Medical School, graduating *magna cum laude* as well.

Vesell did his postdoctoral training at Rockefeller University with several Nobel Prize winners and at Peter Bent Brigham Hospital in Boston. He then met his late wife, Kristen Peery Vesell, while they were both working at NIH.

In 1968, Vesell became the founding chair of pharmacology at the Penn State Health Milton S. Hershey Medical Center, where he served as chair for 32 years. He served as assistant dean for graduate education for 22 years and was recognized as an emeritus and Evan Pugh professor, the university's highest honor.

Vesell published more than 350 articles on pharmacogenomics and received many awards and honorary degrees including an honorary degree from both Penn State University and Marburg University in Germany. The genetic codes on the walls of the Penn State Institute for Personalized Medicine represent his genes.

He is survived by two daughters, Liane Vesell of Boca Raton, Fla., and Hilary Vesell of Hershey, Pa.

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 1-866-833-5433 or email vaccines@nih.gov. Read more online at <https://go.usa.gov/xQGp2>. Se habla español.

Study Needs Heavy Drinkers

Are you a heavy drinker? NIAAA researchers are seeking research volunteers for a study testing a medication that may reduce cravings for alcohol. There is an inpatient stay for approximately 3-4 weeks. Compensation is provided. For more information, call the Clinical Center Office of Patient Recruitment, 1-866-444-2214 (TTY for the deaf or hard of hearing: 1-866-411-1010). Read more online at <https://go.usa.gov/xQjhb>. Refer to study 16-AA-0080.



Damage to Inn Roof Gets Attention

During repairs to its roof, the Children's Inn at NIH sustained structural damage on Aug. 21, forcing temporary evacuation of the facility while engineers checked out the problem. The next day, cranes (above) were used to remove construction materials from the damaged roof. The problem occurred when a roofing contractor placed a large amount of construction material on the roof, causing it to sag. Inn residents were relocated to area hotels at the time of the accident and 10 apartments were rented to accommodate families. The facility partially reopened by week's end; 23 of 59 rooms were deemed safe to occupy. NIH facilities staff will determine the cause of the sagging, which occurred atop the inn's bistro. Meanwhile, the inn asked for community support in sponsoring meals, making donations, making goodie bags for families and providing other needed items. For more information on inn emergencies, visit <http://childrensinn.org/emergency/>.

PHOTO: RICH MCMANUS

'FROM HERE TO ETERNITY' Old Movie Projectors Find New Home in Florida

PHOTOS: CHIA-CHI CHARLIE CHANG

During recent demolition of the E-wing of Bldg. 10, workers came across two old movie projectors on the mezzanine level of the old 14th-floor auditorium. Recognizing that NIH might have objects of value, the Office of Research Facilities prevented the projectors from ending up in a dumpster and have located a home for them.

You might say they are going *From Here to Eternity* (which won best picture in 1953, the year the Clinical Center opened).

"The movie projectors were used in the large auditorium for movie nights on the big screen," said Holly Parker, a recreation therapist at the Clinical Center. "Arnold Sperling was the founder of the recreation therapy program at the Clinical Center and started the movie nights for patients. We used to get the movie reels delivered by mail. We also had a popcorn machine that was a favorite for patients."

Parker's colleague Debbie Marcus, who has been a recreation therapist at the CC for 40 years, adds, "The movies were ordered from a company

called Swank Motion Pictures. Our movie nights were scheduled once a month."

Marcus said that on the 14th floor, movies were run by a department that was a predecessor to the hospital's IT department.

"After the evening of the movies on the big screen in the 14th floor auditorium, the films were brought down to the patient units and shown in solariums and day rooms using a mobile projector to those patients who were unable to attend the general showing.

"The popcorn machine was one of those large industrial ones like you would find at a fair," she continued, "and we made it fresh throughout the movie so patients also enjoyed the aroma of a movie theater as well."

Back in those days, recreation therapy was part of the Patient Activities Department, under Sperling's direction. Today it is part of the department of rehabilitation medicine.

Brad Moss, ORF communication director, searched for takers for the old RCA projectors and found a nonprofit called Coral Gables Art Cinema in Coral Gables, Fla., which collects antique film equipment. The transfer of the machines is due to take place soon.—**Rich McManus**



ABOVE: During demolition of the E-wing in Bldg. 10, workers came across these old movie projectors, which once entertained audiences on the 14th floor of the Clinical Center. The antique items will find a new home in Coral Gables, Fla., thanks to the legwork of Brad Moss, communications director for ORS/ORF.

Photos in this column show details of the old RCA projectors, and the portable projector (circa 1974) that was used to screen films for smaller audiences throughout the hospital. Movies for patients was an innovation of the old Patient Activities Department, which is now a part of the CC department of rehabilitation medicine.

