TRACKING ‘DIGITAL EXHAUST’
Digital Disease Detection Needs Boost, Brownstein Says
BY RICH MCMANUS

The current global coronavirus pandemic is going to be a poster child for all sorts of future public health preparation, but perhaps nowhere more actionably than in real-time surveillance of an infectious disease as it explodes across the world.

“Every domain except health care has data—shopping, travel, news, entertainment, learning—that helps with our decision-making,” said Dr. John S. Brownstein, professor of biomedical informatics at Harvard Medical School and chief innovation officer at Boston Children’s Hospital. “Covid-19 has put a real focus on the inadequacies of public health data collection.”

Brownstein offered a whirlwind overview of how digital disease detection can be improved at the National Library of Medicine/Medical Library Association’s annual Joseph Leiter Lecture on Aug. 11.

“What data streams,” he asked, “can we tap into that unwind the hierarchical—and time-consuming—structure” that governed how the world came to know about a novel coronavirus that was first publicly reported on Dec. 30, 2019, when 7 patients in Wuhan, China, came down with a mysterious illness?

Early reports were linear and slow, arising from the public, to health care workers, to laboratories, to ministries of health (such as the CDC) and finally to world bodies such as the WHO.

“Our view is that all stakeholders in public health should have access immediately,” said Brownstein. Monitoring public health threats should be as obvious and simple as whipping out your smartphone to check the weather, he said.

“Why this doesn’t happen in public health baffles us, right?” he continued. “A National Weather Service for disease outbreaks is something people keep talking about. But we lack the underlying data sets, we lack...”

WHAT HAPPENS IN VAGUS
Experts Expound on Interoceptive Processes
BY DANA TALESNIK

Feeling thirsty or tired? With every breath, heartbeat and hunger pang, there’s a vast, intricate maze of neural circuits communicating these signals and sensations between your organs and your brain.

Research into these pathways and how they can be modulated by different practices and techniques—from yoga to electrical stimulation—can...
2020 NIH Director's Awards Now Online

An NIH Director's Award is the most prestigious non-monetary award at NIH to recognize the outstanding achievements of all institutes, centers and offices. Each nomination undergoes a rigorous review process that includes each institute/center director, the NIH awards review committee and selection by the NIH director for special recognition.

Historically, the in-person ceremony provided an opportunity to showcase stellar service in the areas of research, administration, technical and clerical support, mentorship, clinical care, Commissioned Corps, work/life and well-being and equity, diversity and inclusion. This year, the remarkable accomplishments of 660 NIH staff from the 2019 calendar year are presented in a virtual format. The site https://go.usa.gov/xGm6k was developed in partnership with IC leadership across NIH.

Nominations for the NIH Director's Award are accepted from late fall through mid-winter and should be based on accomplishments fulfilled during the last full calendar year (January–December). Any NIH employee with familiarity of the work performed either by an individual or group can nominate. Nominations for the 2021 NIH Director's Awards will open soon and must be entered through the electronic honorary awards and ranking system at https://go.usa.gov/xGm6Q.

Email nihawards@od.nih.gov for more information on the nomination process.

5th NIGMS Early Career Investigator Lecture, Oct. 14

Dr. Michael D. L. Johnson, an assistant professor in the department of immunology at the University of Arizona, will give the NIGMS Director’s Early Career Investigator Lecture on Wednesday, Oct. 14 at 1 p.m. via Zoom and NIH videocast. The lecture is open to everyone in the scientific community.

During his talk, titled “Microbes, Metals, Music and Lessons in Disproving Your Hypothesis,” Johnson will describe his research on how bacteria maintain homeostasis within the metal milieu. He hopes that understanding how bacteria interact with metals during infections will identify novel therapeutics strategies against bacterial infection.

After a 30-minute lecture, Johnson will answer questions from participants about his research and career path.

This annual series highlights the achievements of NIGMS’s early career grantees. It is designed to introduce students to cutting-edge research and inspire them to pursue careers in the biomedical sciences.

NIH trainees are encouraged to watch via Zoom and participate in the live Q&A. For more details, visit https://www.nigms.nih.gov/News/meetings/Pages/2020-nigms-directors-early-career-investigator-lecture.aspx.

Segre Set for Roberts Lecture, Nov. 3

NHGRI senior investigator and Translational and Functional Genomics Branch chief Dr. Julie Segre will present “Human Microbiome: Friend and Foe,” the 2020 Anita B. Roberts Lecture, on Tuesday, Nov. 3 from 12:30 to 2 p.m.

Segre’s research integrates high-throughput sequencing, algorithm development and clinical studies to explore the microbial diversity of human skin in both healthy and disease states. Her team established the first topographical maps of human skin bacterial and fungal diversity, enabling the study of alternations in those populations that are associated with eczema and other microbial-associated infections.

Segre’s laboratory also integrates genomic tools to track hospital-acquired infections, model outbreaks, monitor evolution of antibiotic resistance and develop risk assessment strategies.

She is a fellow of the American Academy of Microbiology and the National Academy of Medicine and she received the Service to America Medal in 2013.

Segre is also an outstanding mentor and currently serves as a member of the NIH woman scientist executive committee.

The seminar series is dedicated to the memory of Dr. Anita B. Roberts, former chief of NCI’s Laboratory of Cell Regulation and Carcinogenesis. Lectures highlight outstanding research achievements of women scientists in the NIH Intramural Research Program. The virtual talk will be available via NIH videocast at https://videocast.nih.gov/watch=37780.

To arrange sign language interpretation, contact Joy Jackson Farrar or Dee Andrews at jacksjoy@ors.od.nih.gov or dandrews@od.nih.gov.

Fauci Receives 2020 Lienhard Award

The National Academy of Medicine has named NIAID director Dr. Anthony Fauci as the recipient of the 2020 Gustav O. Lienhard Award for Advancement of Health Care.

Fauci is honored for his role as a leader of federal research and policy on infectious diseases and, in particular, for his deft, scientifically grounded leadership in shaping an effective response to the Covid-19 pandemic.

The award will be presented at NAM’s annual meeting, held virtually for the first time ever, on Oct. 19.

Fauci is the 35th recipient of the Lienhard Award. Given annually, the award recognizes outstanding national achievement in improving personal health care in the United States.

The Lienhard Award is funded by an endowment from the Robert Wood Johnson Foundation. Dr. Gustav O. Lienhard was chair of the foundation’s board of trustees from the organization’s establishment in 1971 to his retirement in 1986.

2020 Anti-Harassment Training Launched Online, Must Be Taken by Dec. 14

As part of its continued commitment to achieving a harassment-free work environment, NIH recently launched the 2020 anti-harassment training. The goals are to educate individuals in the workplace to prevent harassment; raise awareness of what constitutes harassment and the consequences of harassing behavior; and stamp out instances where harassing behavior may exist. The online training is mandatory and replaces the No FEAR and Prevention of Sexual Harassment (POSH) training.

All NIH federal employees, trainees, fellows and contractors are required to take the training annually. The 2020 training must be completed by Dec. 14. New hires must complete it within 90 days of onboarding. Failure to comply with the training will result in disablement of a person’s active directory account until the requirement is met. Anyone whose active directory account is disabled will be unable to sign into their computer or access emails.

To learn more about EEO mandatory training, visit the Office of Equity, Diversity and Inclusion website at https://www.edi.nih.gov/training/mandatory-training.
CC Offers Asymptomatic Testing for SARS-CoV-2 to NIH Staff

BY ERIC BOCK

The Clinical Center is now offering asymptomatic testing for SARS-CoV-2 to all staff, including those who are not yet eligible to return to their physical workspaces. Although the program is voluntary, employees are strongly encouraged to participate.

“The main purpose of the testing program is surveillance,” said CC CEO Dr. James Gilman. “With surveillance, the more you test, the more data you have and can figure out what’s going on in the hospital.”

The CC’s department of laboratory medicine has the capacity to conduct 5,000 tests per week but is currently conducting only 1,000 to 2,000 per week. Most CC staff have been tested, on average, 3 times over the past few months.

“We have a lot of unused capacity,” Gilman said.

As the CC gets busier and accepts more patients, testing helps to ensure the safety of both patients and staff. Patients don’t have to worry about contracting a virus after they’re admitted to the hospital. Staff don’t have to worry about getting sick at work.

Asymptomatic testing helps identify people who have Covid-19 but aren’t presenting symptoms. “If we find people who are infected and send them home, we decrease the likelihood they will infect someone else,” Gilman said.

Since the testing program began in late May, he noted, “We’ve had no incidents to date of Covid-19 transmission from staff to patients.” The CC has also helped to develop testing programs for staff at NIEHS in Research Triangle Park, N.C., NIDA and NIA in Baltimore, NIAID in Hamilton, Mont., and NIDDK in Phoenix, Ariz.

Testing for SARS-CoV-2 involves a traditional nasopharyngeal swab, which looks like a 6-inch Q-tip. The swab is inserted through the nose to the back of the throat, rotated several times and left in place for 10-15 seconds.

“Psychologically, having your mid-turbinate area swabbed seems to bother people,” said Gilman, who gets tested weekly.

To increase participation, the CC now offers Covid-19 saliva tests. “We hope that will increase the acceptance of testing, which will increase the number of people who get tested and the frequency with which people are willing to get tested,” he added.

In addition to surveillance testing, the CC has taken other infection control measures to prevent the spread of Covid-19. Staff stay at least 6 feet away from each other, wash their hands often, don’t attend large meetings and stay home if they are sick. All patients and visitors are screened for symptoms at the hospital entrance.

“From our perspective, not enough staff are volunteering to get tested. We really want more people to take advantage,” Gilman concluded. “We encourage staff to get tested every week.”

To sign up for asymptomatic testing for SARS-CoV-2, NIH’ers can visit https://clinweb.cc.nih.gov/cct. Those who sign up must go in either the CC’s north or south entrance. Upon entry, staff will be temperature-screened and given a surgical mask, which must be worn at all times. They should then proceed directly to the 5th floor atrium area to check in for the test.

“From our perspective, not enough staff are volunteering to get tested. We really want more people to take advantage. We encourage staff to get tested every week.”

~DR. JAMES GILMAN

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ON THE COVER: Tissue Chip in Space. An example of a tissue chip—research supported by NCATS.

IMAGE: JOSH VALCARCEL, NASA

The NIH Record

This image depicts a test tube with viral transport media that contains a patient’s sample to be tested for the presence of SARS-CoV-2, the virus that causes Covid-19.

PHOTO: CDC/JAMES GATHANY

Dr. James Gilman

NIH
National Institutes of Health
Turning Discovery into Health
access to APIs [Application Programming Interfaces, a software system that allows two applications to talk to each other], there is no ecosystem of tools that you can turn to.”

It’s not that the clues aren’t everywhere, it’s that no one’s aggregating them, he argued. “People move through the world and they have a ‘digital exhaust,’” said Brownstein. “They search online, they tweet, they use their Fitbit. There is a subset of your digital exhaust that is health-related. We need to tap into that data, at scale. If you aggregate it, you can get amazing insights about population-level events.”

Fifteen years ago, Brownstein and others envisioned such an early alert system. Using funds from NLM, they created HealthMap, with the goal of tapping into the huge troves of online data.

The effort now includes 171 public and private sources, 15 languages and more than 200,000 websites.

“It can tease out important events,” said Brownstein, “but we need to structure the massive noise of data.” Two common tools for modern librarians—natural language processing and machine-learning—“help tag the information churned through daily on HealthMap. This is how the WHO learned of the alarming spread of Covid-19, along with ProMED [the Program for Monitoring Emerging Diseases, run by the International Society for Infectious Diseases].”

**Sites in place before covid**

These tracking sites were in place well before Covid-19. Examples of their utility include:

† Detection of H1N1 (swine flu) in 2009 in Veracruz, Mexico, which enabled authorities to track the spread from country to country.

† Five years later, the same technology identified H7N9 flu in China. Brownstein suggested that parsing of data from Facebook and Twitter could be the next step in bolstering digital epidemiology.

† Bots knew that Ebola was coming in West Africa in 2014. “Access to [airline] passenger data out of West Africa could enable rapid threat assessment—where is the disease going next?” said Brownstein. His team built a zoonotic niche map to label high-risk environments where Ebola might flourish.

† In 2016, Zika virus expansion was tracked by digital sleuths.

The technology is not foolproof. “We found that tracking flu through Google search query data did a poor job on H1N1,” Brownstein reported. However, “Wikipedia is incredibly valuable in tracking influenza, just by counting the page views seeking flu data.”

Other unexpected klaxons of public health issues include:

† Open Table, the online reservation system “has been valuable in Covid-19,” said Brownstein. The availability of table reservations is a predictor of flu-like illness; cancellations are an indicator of social disruption.

† Yelp reviews. Brownstein said that about 10 percent of all Yelp reviews relate to food-poisoning. “That’s an incredibly valuable health care source.”

† Through a partnership with Twitter, Brownstein and colleagues found that “many people, surprisingly, tweet about their diarrhea and food-related issues. We captured that information online from millions of posts and built a tool for public health. We created a social media dashboard for public health, to discuss food-poisoning data...There was a huge number of foodborne illness searches in the wake of Hurricane Harvey.”

**More traditional platforms**

Platforms that are more traditional in structure and intent include:

† Google Mobility Project, which collects data from 300 million users from 243 countries/territories, representing 65 percent of Earth’s habitable surface. “The goal is to develop a global human movement typology that can track the spread of disease,” said Brownstein.

† Crowdsourcing, or “putting the public back in public health,” on sites such as Flu Near You, where 100,000 users report weekly on their symptoms.

† Covid Near You—a collaboration with Amazon, Google, Apple and others—has already been deployed in the U.S., Canada and Mexico, attracting more than 1 million users in the U.S. alone. A symptom-based tracker, it has been “incredibly effective at identifying [pathogen] emergence in populations, determining age-based attack rates, etc.” said Brownstein. There are plans to merge the flu and covid versions.

† EpiCore, already in use for Covid-19, which taps into a network of experts. “Essentially, it’s a Bat Phone for epidemiologists—an information exchange,” said Brownstein. “It pushes information to stakeholders like WHO and the CDC.”

† Health care chat boxes. “This is the next iteration of patient-engagement tools,” said Brownstein. The Symptom Checker, for example, is a self-assessment questionnaire. “These tools are providing an incredible level of diagnostic accuracy, as well as triage accuracy—shifting care to the right place, anywhere from the ER to a telemedicine visit...It also helps with surveillance. There’s been massive growth in these tools as covid has emerged.”

New platforms include Alexa, the voice-activated search tool. “If you’re using them in your consumer life, you can use them in health care as well,” Brownstein said. Other online platforms include KidsMD, to quickly determine the level of care a patient needs, and Flu Doctor, which is also applicable to covid; it is expected to help with vaccine effectiveness and side-effect reporting, and help counter misinformation.

With the coronavirus pandemic, Brownstein said his team has been “heads-down for the last half year.” They are using data-mining tools to track spread, but are limited by scans of news and social media. But what began as a small volunteer effort in January has now become a massive
enterprise.

“We’ve built a global repository of cases, with many partners around the world [including Baidu, the Chinese version of Google]. We used it to measure the impact of the lockdown in China. It proved that lockdowns are effective.”

**New tools and tricks**

The big new tool is Global.health, which launched this summer. Although built as a Covid-19 data science initiative, it is expected to be a boon in future pandemics. A collaboration between Google and a wide range of institutions, it will make public health data freely available in real time.

Even satellite data—photos taken from space—has a public health application. By comparing images of parking lot usage at hospitals in Wuhan taken a year before the outbreak, an uptick could be found last fall, indicating more visits, more need for care. Parking lot photos have helped predict flu season in Venezuela, too, reported Brownstein.

A partnership with the popular survey software SurveyMonkey, offered as an option for those doing other kinds of surveys, showed Brownstein and his team that “half of the people we surveyed in the U.S. wouldn’t get a vaccine as soon as it became available; 1 in 8 would not want to get it ever. Those age 75 and older are the most eager to get it right away, without hesitation.”

The researchers also surveyed mask-wearing, an important avenue to lowering R-naught, or the reproductive number, a measure of virus transmission. At least half the people in a population need to be masked to budge the number toward viral extinction.

Aware that Covid-19 has disproportionately ravaged minority communities, Brownstein’s team is also tracking access to testing, including travel time to the nearest testing center. They will apply Vaccine Finder, a tool begun for H1N1 flu, to Covid-19, to make testing more convenient.

The Joseph Leiter NLM/MLA Lectureship was established in 1983. Brownstein’s full, and rather dizzying, version is available at https://videocast.nih.gov/watch=38269.

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**D’Souza Selected as Next NIDCR Director**

On Aug. 13, NIH director Dr. Francis Collins announced that he selected Dr. Rena N. D’Souza as next director of the National Institute of Dental and Craniofacial Research.

A licensed dentist, D’Souza is currently assistant vice president for academic affairs and education for health sciences at the University of Utah, Salt Lake City. There she also serves as a professor of dentistry, the Ole and Marty Jensen chair of the School of Dentistry and professor of neurobiology and anatomy, pathology and surgery in the School of Medicine and the department of biomedical engineering. She is expected to begin her new role as NIDCR director later this year.

“Dr. D’Souza is renowned for her research in craniofacial development, genetics, tooth development and regenerative dental medicine,” said Collins. “She has worked as a proponent for NIH for decades, serving on critical advisory committees and as an expert consultant on multiple projects.”

D’Souza will oversee the institute’s annual budget of more than $475 million, which supports basic, translational and clinical research in areas of oral cancer, orofacial pain, tooth decay, periodontal disease, salivary gland dysfunction, craniofacial development and disorders and the oral complications of systemic diseases.

D’Souza’s research focuses on developmental biology and genetics; matrix biology; biomaterials, tissue engineering and stem cells; and clinical research. Her group’s discovery that a novel mutation in PAX9 was responsible for a severe form of human tooth agenesis opened a new field of research to discover genes and mutations as well as therapies for common human inherited disorders of the craniofacial complex. The finding, published in Nature Genetics, was highlighted in the Jan. 25, 2000, issue of the NIH Record (p. 3 of https://nihrecord.nih.gov/sites/recordNIH/files/pdf/2000/NIH-Record-2000-01-25.pdf).

She was selected to be the inaugural dean of the University of Utah’s School of Dentistry, which was established in 2012. She is currently the elected chair in the dentistry and oral health sciences section and elected as a fellow of the American Association for the Advancement of Science. She also is a former president of the American Association for Dental Research and the International Association for Dental Research, a fellow of the American College of Dentists and the recipient of the 2017 American Association for Dental Research Irwin D. Mandel Distinguished Mentoring Award. D’Souza served on the advisory committee to the NIH director in 2013-2014, and on NIH study sections. She is a devoted mentor and champion of diversity in the biomedical research workforce. Since 1985, she has served as a volunteer dentist for women in need and people struggling with homelessness in Salt Lake City, Dallas and Houston.

D’Souza received her bachelor’s degree in dental surgery from the University of Bombay, India, after which she completed her general practice residency. She earned her D.D.S., Ph.D. and master’s degree in pathology/biomedical sciences from the University of Texas Health Science Center in Houston.
Interoception
CONTINUED FROM PAGE 1

improve physical and emotional well-being.

Breathing, heartbeat, cravings, fatigue, even pain: these internal processes are part of a mind-body connection called interoception, which encompasses our ability to sense and regulate signals from inside our bodies. Sometimes, we’re not even aware they’re happening.

“Importantly, these processes of sensing, interpreting and integrating include both conscious and unconscious phenomena, factors and mechanisms,” explained NCCIH director Dr. Helene Langevin during introductory remarks at a recent NCCIH virtual webinar.

Focusing on the conscious aspects, Dr. Wolf Mehling, professor of clinical family and community medicine, University of California, San Francisco, said numerous studies have shown that mindful attention toward physical sensations from inside the body changes brain rhythms. He discussed ways to measure interoceptive awareness—how we perceive, sense and respond to the inner workings of our bodies—and how this can be modified with mind-body approaches.

Mehling led an NCCIH-supported team in developing the MAIA scale (multidimensional assessment of interoceptive awareness), a set of questionnaire scales related to self-perception. Physiological tests are important, he said, “but we also should use questionnaires because they’re able to differentiate the [various] dimensions of interoception.”

One key MAIA scale is self-regulation, the ability to regulate distress by paying attention to body sensations, such as our breathing. Mehling cited studies using meditation, yoga and tai chi—incorporating breath awareness—that resulted in reduced pain, fatigue, anxiety and depression.

In a study of patients suffering from chronic low-back pain, three elements on the MAIA scale proved particularly useful: emotion awareness, self-regulation and body-listening.

“These 3 were the only scales out of 19 different physiological questionnaires that were able to predict treatment outcomes,” said Mehling.

Another way to probe interoception is to modulate interoceptive pathways via the vagus nerve, the longest cranial nerve, which travels from the digestive tract to the brain. Dr. Eleni Frangos, an NCCIH postdoctoral fellow, focused on afferent pathways, neural circuits ascending from a sense organ toward the brain or spinal cord, or between brain regions.

Studies have shown that focusing on sensations arising from our organs activates the insula, and these interoceptive signals converge and integrate with emotional and cognitive networks across the brain. This complex web of interoceptive awareness has been confirmed in numerous studies, including heartbeat and breathing detection tests.

Electrical stimulation of the vagus nerve can activate multiple brain regions that are involved in interoception. An invasive approach involving implanting electrodes, vagus nerve stimulation (VNS) has been used in patients with treatment-resistant depression and epilepsy and has shown promise in decreasing pain sensation.

“There is plenty of evidence that suggests vagal stimulation modulates affect [or mood] and so much so that it’s an FDA-approved treatment option for refractory depression,” said Frangos. “There’s also evidence that it’s beneficial for other treatment-resistant disorders like OCD, panic disorder and post-traumatic stress disorder [PTSD],” for up to 4 years after implantation.

Newer noninvasive tools can access vagal afferent nerve fibers with a handheld device used externally on the neck or ear. Preliminary research shows beneficial effects in some patients with major depression and anxiety; improvements in memory, learning and reaction time; and reductions in headache pain, said Frangos.

While stimulation of the vagus nerve may reduce pain, so too can mindfulness. “Taking someone’s attention away from a painful stimulus will decrease pain perception, and these psychological factors influence pain perception,” she said. “Manipulating emotion affects pain unpleasantness, while manipulating attention affects pain intensity.”

For the descending (efferent) neural pathways that wind down from the brain to innervate organs and tissues throughout the body, there are various ways to measure this nerve activity. Reliable measurements are important, explained Dr. Jeanie Park,
associate professor, Emory University School of Medicine. Chronic overactivity of this efferent sympathetic nervous system can have serious consequences leading to high blood pressure, heart failure or kidney disease.

“Microneurography is the gold standard method by which we can measure and quantify sympathetic activity directly, in real-time, from awake humans,” said Park.

Developed 50 years ago, the technique involves inserting a microelectrode into a peripheral nerve to record sympathetic nerve activity directed to the blood vessels that supply the muscle (i.e., muscle sympathetic nerve activity). This technique offers insights into the effects of modulating interoceptive pathways on the sympathetic nervous system.

“Not only can we use microneurography to characterize baseline resting differences between different patient groups,” said Park, “but we can also study the reactivity of the sympathetic nervous system to stress.”

For example, muscle sympathetic activity tends to be elevated in response to stress in veterans with PTSD. “This is important,” she said, “because exaggerated sympathetic reactivity is associated with increased risk of hypertension and cardiovascular disease.”

Using a biofeedback device, slow breathing—5 or 6 breaths per minute—strikingly lowered the veterans’ muscle sympathetic nerve activity and blood pressure. The mechanisms may include unconscious components (such as activation of baroreceptors, nerve endings sensitive to changes in blood pressure) and a conscious component, such as increased breathing awareness.

Vagus nerve stimulation also inhibits sympathetic nerve activity. A new paper recently reported the first successful vagus nerve recordings using microneurography, showing the nerve can be directly accessed and recorded from awake humans. Said Park, “It really opens up a lot of new, exciting opportunities to study both afferent and efferent vagus nerve activity.”

Further study into interoceptive pathways and how to manipulate them can lead to effective new therapies and preventive strategies. There are potential applications across medicine, from neurology to mental health, pain and addiction, gastrointestinal to cardiovascular health, and across the lifespan.

TONNAGE OF DUNNAGE

**Big Doings Behind, Atop the Clinical Center**

As part of E-wing renovation at the Clinical Center, a 600-ton crane was used to hoist steel to the roof of Bldg. 10 during the last two weekends of August.

The steel, known as dunnage, was used to support rooftop mechanical/plumbing items such as exhaust ductwork stacks and fans, energy recovery units, piping, framing, air-cooled chillers and an air-handling unit.

The project was coordinated by Jeanne Keegan of the Division of Design and Construction Management, Office of Research Facilities.

At left, a 600-ton crane lifts dunnage steel to the Bldg. 10 roof. The crane worked for two full weekends and at night in order to provide a safe environment for occupants. At right, the crane parts had just been assembled and the crane is being prepared to hoist material to the roof.

Workers receive the dunnage steel on the roof for assembly. The dunnage was installed to support mechanical equipment and large piping.
Burgess

CONTINUED FROM PAGE 1

co-director of the Sleep and Circadian Research Laboratory at the University of Michigan and a grantee of NCCIH, NHLBI, NIMH and multiple other NIH components.

She focused on the most well-studied aspect of light and health: the circadian clock, an “ancient physiological system” that is largely determined by genetics. Its two parts are the central circadian clock, located in the hypothalamus, and a network of peripheral circadian clocks found in almost every cell, tissue and organ. The latter clocks have local control over many of our biological systems, such as those for behavior, hormones, inflammation and immunity. If the circadian system were an orchestra, Burgess said, the central clock is the conductor and the peripheral clocks are the instruments.

In about 70 percent of us, the central clock takes a little more than 24 hours to complete one cycle. This creates a tendency over time to “phase delay” (i.e., move the circadian clock later). How can affected people get and stay in sync with an environment running on a 24-hour clock? Researchers are exploring strategies to “phase advance,” including by manipulating the properties of light and exposure to it. Lifestyle measures may also help.

Since the 1980s, light therapy has been a mainstay of treating seasonal affective disorder (SAD), a type of depression that usually starts in late fall and early winter (because of less sunlight) and often eases in the longer days of spring and summer. Burgess offered some suggestions on how viewers could leverage their light exposure to benefit health. For example, “for those of us who need to shift earlier (i.e., phase advance), morning light is the most important light we receive during the day. In contrast, evening light, light before bed and light during your sleep episode will shift you later.”

“For many of us, evening light is not our friend,” she continued. “But we know there’s a lot of light pollution at night, and as human beings we tend to engage in behaviors that are not always the best for us. Ninety percent of Americans use a light-emitting technology device in the hour before bedtime, according to one survey. So does it really matter whether our clock and sleep times shift a bit?”

The answer is yes, over time. The term “social jet lag,” coined by Dr. Till Roenneberg at Ludwig Maximilian University in Munich, Germany, describes a syndrome similar to normal jet lag but arising from lack of alignment between a person’s biological and social clocks.

“Making subtle but chronic shifts of 2 hours or more in your circadian timing may have long-term health consequences,” Burgess cautioned.

So far, cross-sectional studies have found links to higher risk for depression; greater likelihood for alcohol and caffeine use and smoking; higher body mass index; and negative changes in some common measures such as resting heart rate, C-reactive protein, high-density lipoprotein cholesterol and triglycerides. This situation might reflect some self-medication for difficult symptoms of social jet lag. Results of longitudinal studies are pending.

Light also has physiological effects beyond its effect on circadian timing. For example, light suppresses melatonin. In many studies, lower levels of melatonin secretion overnight were predictive of development of breast cancer, hypertension, insulin resistance or type 2 diabetes in participants. An emerging literature suggests that giving people supplemental melatonin might help suppress systemic inflammatory markers, but this area needs further investigation.

Light may also affect neurotransmitters in the brain. A study conducted by Dr. Lily Yan at Michigan State University found light-dependent increases in serotonin (a chemical important in mood) in many different brain areas of a day-active rodent model.

With respect to chronic pain, one of the speaker’s studies was a small, NCCIH-funded pilot project conducted in women with fibromyalgia. Participants received one hour of bright light treatment either in the morning or evening from a light box. The researchers examined outcomes related to function, pain sensitivity and circadian timing. They found improvements in function and pain sensitivity from both morning and evening light treatments. But those improvements became clinically meaningful only from morning light, also the only light treatment to improve pain tolerance (phase-advancing was offered as a possible mechanism).

A second NCCIH-supported study, in military veterans with chronic low-back pain, found morning light treatment was helpful in reducing pain and suggested possible benefits for post-traumatic stress disorder. Light treatment, Burgess said, is relatively easy to access compared to many other interventions and requires less physical exertion for pain patients. It should also be studied in treatment combinations.

To promote wellness, Burgess suggested the following:

• Try to get more light during the day—outdoors if possible, with 30 minutes to an
hour as a typical amount. “Morning light is good for most of us,” she said. However, two groups should first consult their health care providers: older adults (because their circadian rhythms normally shift earlier in aging) and people with bipolar disorder (as extra light might be overly stimulating).

• Usually, being outside offers brighter light than being inside (although not always). For most people, going outside for light as soon as possible after waking up is the best time—but if the morning is too busy, one can go out sometime before sunset (weather permitting, of course).

• Exposure to ultraviolet light carries risks to the eyes. You might choose to go without sunglasses for just part of your time outdoors or wear sunglasses the entire time, in which case you will still receive some benefits from light.

• When inside, try to sit by a window, if possible.

• After sunset, minimize your exposure to artificial light. Use distance and dimming—e.g., watching a TV across the room is better than using a cell phone or tablet close to your eyes. The more you dim your evening light, the less you will phase delay (have your circadian cycle move later).

• Don’t use light-emitting devices in the hour before you go to bed.

• Set an alarm for a half hour before you usually go to bed. Retiring at the earlier time will help in obtaining the 7 to 8 hours (at least) of sleep recommended by the American Academy of Sleep Medicine.

• Don’t treat yourself with melatonin without talking to your health care provider first. Underlying medical conditions and potential drug interactions are among the factors to consider.

• People who cannot get outside and don’t have the benefit of a window sometimes consider light boxes. These are available and often less expensive than wearable light devices. If you have an eye disease, talk to your ophthalmologist first before considering a light device, and if you have a mental health diagnosis, especially bipolar disorder, talk to your mental health professional first.

The full lecture is available at https://videocast.nih.gov/watch=37830.
**Biomarkers Could Help Predict Time Needed for Athletes to Recover from Concussion**

A collaborative study conducted by scientists from NIH, the Department of Defense, and multiple academic institutions has identified blood biomarkers that could help predict which athletes need additional time to recover from a sports-related concussion. This collaboration, known as the Concussion Assessment, Research and Education consortium, is supported, in part, by DoD and the National Collegiate Athletic Association.

In this study, conducted at several sites across the U.S., 127 male and female collegiate athletes who had sustained a sports-related concussion were tested at several time points: shortly after injury, when their symptoms resolved, and one week after returning to play. Each athlete had also undergone preseason, baseline testing.

Using an ultrasensitive assay that can detect minute amounts of protein, the researchers tested blood serum from these athletes and identified two blood proteins that were associated with the length of time needed by the athletes to return to play.

Amounts of these two proteins, tau protein and glial fibrillary acidic protein, were found to be significantly different in athletes who needed less or more than 14 days to return.

While further research is needed, the results of this study are an important step toward the development of a test that could help predict which athletes need more time to recover from a concussion before resuming activity.

The study was published in *JAMA Network Open*.

**People with Intellectual, Developmental Disabilities Disproportionately Affected by Covid-19**

The Covid-19 pandemic has taken a disproportionate toll on people with intellectual and developmental disabilities (IDDs), write the directors of the Intellectual and Developmental Disabilities Research Centers Network, a nationwide group funded by NICHD. Their article appears in the *American Journal of Psychiatry*.

A large number of people with IDD who require in-person care have lost the support of trained caregivers and community service providers due to the pandemic. The authors note that the Centers for Disease Control and Prevention and others have issued guidelines for group homes, schools and others entrusted with the care of people with IDD. It is vital to ensure that when they return to work, care staff exercise techniques and procedures to protect their clients from infection, the authors write.

Moreover, people with IDD depend on caregivers and loved ones to help them bridge gaps in intellectual and communication abilities. In the absence of this human contact, the authors call for virtual care and support, where viable. Those who cannot benefit from screen-based supports should be prioritized to receive in-person services.

Suspension of classroom time also disproportionately affects children with IDD, who often require special educational services, increased teacher-student ratios and specialized interventions, many of which need to be administered in person, the authors note. It is difficult for families to take on these tasks, and qualified in-home surrogates should be mobilized whenever possible to meet this need and to support parents’ efforts.

Also, people with IDD often cannot verbalize their symptoms during telemedicine appointments, and physicians need to use their best judgment in providing in-person care for them when necessary, according to the authors.

The article emphasizes that people with IDD who are infected with Covid-19 should receive equal access to testing and appropriate medical care.

**Vaping, Marijuana Use Rose in College-Age Adults**

Vaping marijuana and vaping nicotine rose sharply in the past 3 years among college-age (19-22 years old) adults, according to 2019 survey results from the Monitoring the Future (MTF) study. The percentage of college students who said they vaped marijuana in the past 30 days rose from 5.2 percent in 2017 to 14 percent in 2019. The corresponding percentages for their non-college-attending peers increased from 7.6 percent in 2017 to 17 percent in 2019.

MTF, an ongoing study of the trends in substance use by adolescents and adults in the United States, is funded by NIDA. The survey is conducted by scientists at the University of Michigan’s Institute for Social Research.

The percentage of adults ages 19 to 22 who vaped nicotine also rose dramatically between 2017 and 2019. In 2017, 6.1 percent of college students and 7.9 percent of those not in college said they vaped nicotine in the past month, rising to 22 percent and 18 percent, respectively, in 2019. These increases in vaping marijuana and nicotine are among the largest increases in use for any substance reported by the study in its 45-year history.

“Among the changes in recent years has been a rise in the use of vaping devices and liquid containing nicotine or other substances such as marijuana,” said NIDA director Dr. Nora Volkow. “Many young people may view vaping as ‘safer’, but the reality is that nicotine is highly addictive, and cannabis can also be addictive, particularly in younger adults for whom the brain is still developing.”

The MTF study has been annually tracking substance use among college students and non-college adults since 1980. Other highlights from the 2019 survey:

- Cigarette smoking continued a downward trend; binge drinking showed no significant changes; and prescription opioid misuse continued to decline, as did amphetamine use.
Longtime Engineering Authority Eden Mourned

Dr. Murray Eden, a renowned pioneer in the field of biomedical engineering and imaging and former director of the trans-NIH Biomedical Engineering and Physical Science Program for 18 years, died peacefully in his sleep on Aug. 9. He would have been 100 years old on Aug. 17.

Eden was professor emeritus in electrical engineering at MIT and worked at the intersection of mathematics, engineering, biology and medicine during the infancy of biomedical engineering.

In 1970, he co-authored the book *Engineering and Living Systems* with physician Dr. David D. Rutstein in which they described their new, interdisciplinary vision for health care in the future. Eden is also credited with foundational work in pattern recognition and its application in image processing for medical diagnoses.

Over his long career at MIT and NIH, he collaborated with colleagues from many disciplines and mentored young researchers and students who have gone on to distinguished careers. NIH recruited him from MIT in 1976 to oversee the Bioengineering and Physical Science Branch (then part of the former Division of Research Services, OD), and he dramatically expanded and enhanced the program. The program had a somewhat nomadic existence, moving over the years from DRS to NCCR to ORS and ultimately became the principal initial component of NIBIB’s intramural research program. Eden retired from NIH in 1994.

Under Eden’s inspirational leadership, members of the program collaboratively created numerous bioengineering firsts, ranging in scale from near-atomic resolution to applications for the clinic. These included: the first applications of wavelets to computed tomography; analytical methods (such as using electron microscopy for quantitative imaging of distributions of atomic elements in tissues); mechanical and electrical engineering designs enabling laser capture microdissection; serial block-face scanning electron microscopy; ground-breaking work in pharmacokinetics, including “convection-enhanced” delivery of drugs to brain tumors; analysis of macromolecular interactions by analytical ultracentrifugation; advances in the theoretical underpinnings and implementation of MRI, including critical radiofrequency circuits and “shielded gradients” enabling echo planar imaging; and creation of diffusion tensor imaging.

After earning a B.S. degree in chemistry from the City College of New York in 1941, Eden attended graduate school at the University of Maryland and creation of diffusion tensor imaging (thus began a term of government service spanning more than 50 years). Upon receiving his M.S. in physical chemistry from the University of Maryland, he began work as a biophysicist at the National Bureau of Standards in 1943. During World War II, he worked in the Princeton facility of the Manhattan Project alongside then student Dick Feynman and others, helping produce uranium-235.

He returned to the government as a physicist at the National Bureau of Standards. Six years later, he transferred to NCI as a biophysicist and completed his doctorate in physical chemistry and physics at the University of Maryland. From 1953 to 1955, he returned to Princeton to do postdoctoral work as a Public Health Service fellow and then returned to NIH within the Laboratory of Technical Development, NHLBI. In 1959, he took a job at MIT, where he co-founded the cognitive information processing group and headed it until 1976.

Eden found time over the years to serve as a lecturer, visiting professor or adjunct professor at institutions such as Harvard Medical School, American University, Boston University Law School, Johns Hopkins University, the Swiss Federal Polytechnic Institute at Lausanne and the University of Pennsylvania.

He also had numerous consultancies, including to the director-general of the World Health Organization in Geneva, Switzerland (1963 to 1992), and in 1983 he received the WHO Medical Society medal. He was also one of the principal technical consultants for the symbol standard subcommittee of the Uniform Grocery Product Code Council (1971 to 1974).

“That was the group that established the bar codes you see on all of the products you buy at the supermarket,” Eden said. “It was my idea to put the numbers underneath the code [as a failsafe], and I also picked the typeface for the numbers.”

With a grin he added, “That’s my 15 minutes [of fame], and nobody knows about it.”

Eden loved music and often had resounding classical selections on his radio as he worked. In the 1950s, he played the role of Benny Southstreet in the NIH Hamsters (an employee theater group) production of *Guys and Dolls*.

“One of the many remarkable things about Murray was that he had so many careers,” said Dr. Hank Eden (no relation), who was deputy director of the Biomedical Engineering and Physical Science Program. “He seemed to have known everyone. In fact, framed on Murray’s wall was a piece of paper with equations scribbled on it from Albert Einstein’s wastebasket. [Murray retrieved it when he was a postdoc at Princeton.] Another aspect of Murray’s personality was that, despite all the things he accomplished and the famous people he knew, he was really down to earth. He also had a great sense of humor."

Eden’s personal research focus was pattern recognition and quantification of biomedical images and their efficient storage. “Basically, I’ve been working on trying to model physiological processes,” he once said, “I’m interested in how to make machines do what humans can do because, by studying how to mimic human performance, we will better understand how the human machine operates.”

He leaves a brother, Dr. Alvin Eden of New York City; 5 children, Abigail Eden of Cherryfield, ME; Susanna Eden of Tucson, AZ; Mark D. Eden of Taos, NM; Shirley H. McDaniel, Venice, FL; and John W. Hartle, Juneau, AK; and 7 grandchildren. 

MILESTONES

PHOTO: ABBY EDEN

Looking for Covid-Positive People

NHLBI researchers seek Covid-19-positive patients in the DMV area for a new clinical trial. The study hopes to help researchers understand how coronavirus affects the function of the body’s immune system in controlling the infection. Additionally, researchers want to understand how different organs of the body (such as the lungs, heart, brain and kidneys) respond to the infection from its early appearance to recovery, and whether there are any long-term effects. For details, see https://go.usa.gov/xfcEh. All medical care is at no cost to the participant and compensation for the entire study is provided. Contact NATHX_COVID@nih.gov for more information.

NICHD Recruits Kids for Growth Study

NICHD study seeks children 2-18 years old with growth hormone excess to participate in a research study. Researchers want to see if pegvisomant, a drug that antagonizes growth hormone action, can help children and adolescents with gigantism. See details at https://go.usa.gov/xyqQu. If you are interested in participating, contact the Clinical Center Office of Patient Recruitment at 800-411-1222, TTY for the deaf or hard-of-hearing 1-866-411-1010. Se habla español. Email prpl@cc.nih.gov. Refer to study 19-CH-0071.
Flu Vaccine Clinic for Staff Begins

The Office of Research Services and the Clinical Center will provide free flu shots to staff with a valid NIH identification badge from Sept. 28 through Nov. 6.

This year’s immunization clinic will have some significant changes. Two big differences are that the location on the main campus has changed to the Bldg. 10, B1 cafeteria, accessible from the outside entrance only, and the vaccine will be given by appointment only through an online registration system. Walk-in immunization will not be available.

2020-2021 Immunization Schedule and Registration

**BUILDING 10/B1 CAFETERIA - MAIN CAMPUS SITE**

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<th>Date</th>
<th>Location</th>
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<tr>
<td>September 28 - October 2</td>
<td>Building 10, B1 Cafeteria, South Side. Accessible via entrance from outside only, do not use lobby entrance.</td>
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<td>October 7</td>
<td>Bldg. 10, B1 Cafeteria, South Side. Accessible via entrance from outside only, do not use lobby entrance.</td>
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<td>October 15-16</td>
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<td>October 21-23</td>
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<td>October 26</td>
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<td>October 29 - November 6</td>
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Visit www.foiltheflu.nih.gov to schedule your flu vaccine, VPN or Citrix required.

**WEEKEND HOURS**

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<td>October 24</td>
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**OFF CAMPUS SITES**

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