

MIXED MEDIA MESSAGES

Do Conflicts in Health Communication Shake Your Confidence?

BY CARLA GARNETT

Should I eat fish for better heart health or worry more about the mercury it contains? How about alcoholic beverages—is a glass of red wine good for me or not? When should I start having regular mammograms—at age 40, 45, 50? And should I go annually or every 2 years?

No doubt most of us have confronted health headlines that presented us with conflicting options. What, if any, effect did the conflict have on your confidence in science or medicine? How did media reports factor into your decision?



Dr. Rebekah Nagler of the University of Minnesota discussed conflicting health messages at a recent ODS seminar.

PHOTO: UNIVERSITY OF MINNESOTA

To offer insights on how the public receives and processes such mixed messages, NIH grantee Dr. Rebekah Nagler presented “Conflicting and Controversial Health Information in the Media: Content,

Exposure and Effects,” the final installment in the Office of Dietary Supplements 2019-2020 Seminar Series.

Media frequently broadcast health information that, to Joe and Jane Public, seems at odds, Nagler said, describing the examples above. “In our experience, the conflict and controversy often co-occur, but they don’t always,” she said. “It’s possible to have information that is in conflict, but where there is not necessarily heated dispute or disagreements.”

An associate professor in the Hubbard School of Journalism and Mass Communication at the University of Minnesota, Nagler has conducted research on public health messaging for more than a decade. Her work has been supported by NCI as well as the Office of Research on Women’s Health via its Building Interdisciplinary Research Careers in Women’s Health program.

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Harris Reflects on Decades of Research into Rare Disorder

BY DANA TALESNIK

Severe developmental neuropsychiatric disorders cause patients and their families relentless suffering. Treatment of symptoms



Dr. James C. Harris

may provide short bursts of relief but do little to improve the patient’s quality of life. Determined to improve outcomes for these intractable conditions, investigators have persevered; their longtime research is

SEE **HARRIS**, PAGE 6



Richard Fagerlin

GIVE IT TO GET IT Fagerlin Discusses Economics and Value of Trust

BY RICH MCMANUS

Back when people used to work in offices and reported to bosses and interacted with coworkers—a state that, it is said, will come again—trust was a key component in moving things forward.

Speaking, virtually, on the topic of trust at a time when it is hard to come by amid

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CIT-developed devices deployed to Covid-19 frontlines. See story, p. 12.

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Fitness Challenge Welcomes NIH'ers

Put on your bell-bottoms, grab your favorite cassettes and pack the Polaroid for a fun-filled, nostalgic journey to some of America's most popular out-of-the-way places. NIH is participating in Coast to Coast, a fun and invigorating fitness and walking challenge available to all employees. It is sponsored by Kaiser Permanente.



The challenge started July 21 and runs through Aug. 31. You will be whisked away on a virtual shore-to-shore tour. Coast to Coast will take you across this great land

of ours, stopping at amazing attractions with postcard-perfect vintage and modern images, plus "bet-you-didn't-know" descriptions. Each day you'll visit a new attraction, earning points and "road signs" as you record exercise minutes or steps.

To make this challenge even easier, you can link your own personal tracking device (Fitbit, Garman, etc.) with the Coast to Coast website or mobile app. Your step count will automatically update daily to help you keep pace with the competition and keep track of your personal goals.

Speaking of competition, you won't be alone on your Coast to Coast journey. You will be "competing" with other NIH employees in a race to earn the most points. You can also choose to team up with 3 or 4 other coworkers for a friendly and exciting team competition, even if you're social distancing.

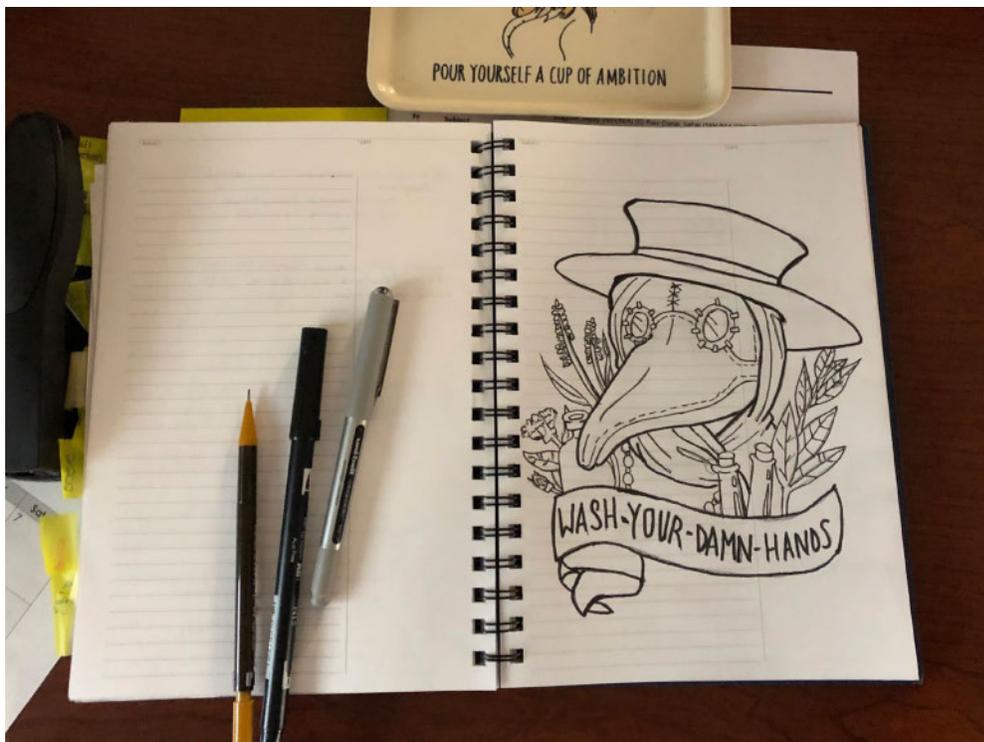
Get ready to move toward a healthier you—register at <https://fedsggetfitmas.coasttocoastwellness.com/#/welcome>.

Food Drive Now at Halfway Point

We are now halfway through this year's Feds Feed Families Campaign. As of June 30, NIH reported donating 140,201 pounds of food.

On June 25, NIH hosted a "Virtual Food Drive" event. Katherine Donnelly, nutrition education specialist from the Capital Area Food Bank, provided an overview of the extent of food insecurity in our region and described which populations are particularly impacted. She explained how local organizations are meeting needs during this uniquely challenging time. At the end of the webinar, Tim Tosten, associate director for program and employee services at the Office of Research Services, provided information on how NIH staff can help fight hunger through the Feds Feed Families Campaign.

For more information on the campaign, visit <https://www.ors.od.nih.gov/FedsFeedFamilies/Pages/default.aspx>. If you have any questions about the effort, contact FedsFeedFamiliesNIH@nih.gov.



"During this pandemic period, I have gone back to drawing," said Sahar Rais-Danai, deputy chief grants management officer at NIAMS. "Although my artwork might have taken a dark turn, I think this conveys an important message. It's definitely getting framed and put up in the bathroom."

We've Seen Your Pets—Now Show Us Your Projects

In the same spirit as the recent *NIH Record* photo series on pets who got us through our teleworking travails, we are now soliciting photos of projects you may have undertaken during the pandemic period, and of which you are proud.

Did you complete a piece of furniture, build a guitar, master the baking of sourdough bread or concoct homemade ginger beer? Did you take up painting, learn bonsai or become a bike mechanic?

Here's the challenge: Send us a photo (high-resolution color digital image) that visually captures your achievement and a caption of 30 or fewer words. Feel free to include yourself in the image.

We will accept submissions through Friday, Aug. 7. Email us at rm26q@nih.gov or cg9s@nih.gov.



Dr. Peter Kilmarx (l), FIC deputy director, drills holes in a log to inoculate with shiitake mushroom spore dowels at home in Bethesda in April. The mushrooms will grow in 6-12 months. The masks (above) were made by his wife, Nichaphat Kilmarx, for their family and friends.

Medical History Matters in Era of Big Data

BY ERIC BOCK

Scientists involved in machine learning often don't know the origins of the datasets they use to write and test algorithms, including where the Pima Indians Diabetes Database (PIDD) came from, explained Dr. Joanna Radin at a recent virtual NLM history talk.

"The history of the PIDD makes political and economic subjectivity visible in ways that are of enormous consequence to practitioners and participants in medical and machine learning," said Radin, associate professor of the history of medicine and history at Yale University.

Machine learning is a sub-discipline of artificial intelligence that dates to the 1950s. Radin explained: "It focuses primarily on algorithms capable of learning or adapting their parameters based on a set of observed data without having been programmed to do so."

In 1987, Dr. David Aha and several graduate students at the University of California, Irvine, built an archive of datasets called the UC Irvine Machine Learning Repository. It offered programmers the ability to download large, well-validated datasets needed to test algorithms.



THANK YOU

Read more at:

[Joanna Radin \(2017\) "Digital Natives: How Indigenous and Medical Histories Matter for Big Data" *Osiris*, 32: 43-64](#)

One of the oldest files in the repository was the PIDD. It became a standard for testing data-mining algorithms in predicting diabetic status. What made the PIDD so valuable is that programmers knew it reliably predicted when people get diabetes.

The Pima, who refer to themselves as *Akimel O'odham*, which translates to "River People," are an indigenous community. Most of the community lives on the Gila River Indian Reservation located in Arizona. In the early 1960s, the institute now known as NIDDK began conducting an epidemiological study of arthritis among the community. The researchers quickly learned that the inhabitants had one of the highest recorded rates of diabetes.

By 1965, Radin said, every resident older than 5 in the study area had been asked to participate in a



Dr. Joanna Radin (above and below) lectures virtually to an NIH audience on Big Data.

longitudinal study of diabetes. Estimates suggest that 90 percent of the reservation enrolled in the study. NIH researchers later worked with computer scientists to digitize long-term patient data.

"Medical information collected has been regarded as a valuable resource for improving general knowledge about the disease," she said.

In the 1990s, Aha, who had been collecting data for the repository, had completed a postdoctoral fellowship at Johns Hopkins. It was around this time that a researcher from the Applied Physics Laboratory, located near Johns Hopkins, came into possession of the dataset.

"What surprises me is that we get from a situation where we're using data collected from indigenous people for diabetes research and, by 2006, the dataset became so standard that it's being used to teach people how to use R, a popular statistical software package," Radin said. "Such uses are purely about teaching people about how to use data."

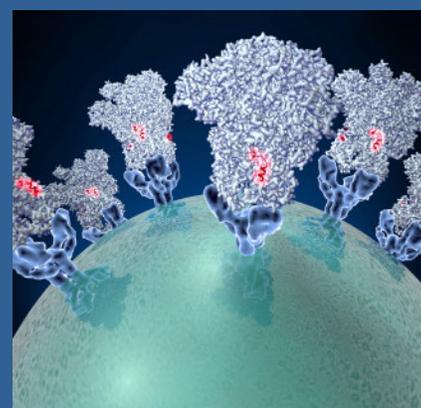
A few years ago, she spoke to an expert in machine learning who was writing an algorithm for New York City's electricity provider to predict where fires might spark in the underground power grid and trigger an explosion of manhole covers. To test and optimize the algorithm, the expert fed it several complex, widely available data sets, including the PIDD.

The story of how participants in an NIH research study on diabetes and how their data was used to refine an algorithm that would predict where a manhole cover would erupt "is exemplary of the history of big data," Radin said.

Today, the use of patient data from all kinds of communities is part of the public health response to Covid-19 outbreaks around the world. Officials are using contact-tracing mobile apps to identify people who might have been exposed to the virus.

While these technologies might help limit spread of the virus, Radin said it's important to think about their implications, given the history of big data. How, for example, will private companies or governments use mobility data in the present and future?

"Sometimes even the best of intentions are upended by the momentum of the technological systems that people find themselves in," Radin concluded. **R**



ON THE COVER: *Coronavirus spike protein structure. Coronaviruses are enveloped viruses responsible for 30 percent of mild respiratory infections and atypical deadly pneumonia in humans worldwide. These pneumonia include those caused by infections with SARS-CoV and MERS-CoV. The coronavirus spike glycoprotein mediates virus entry into cells and represents an important therapeutic target. The illustration shows a viral membrane decorated with spike glycoproteins; highlighted in red is a potential neutralization site, which is a protein sequence that might be used as a target for vaccines to combat coronaviruses.*

IMAGE: DAVID VEESLER, UNIVERSITY OF WASHINGTON

The NIH Record

Since 1949, the *NIH Record* has been published biweekly by the Editorial Operations Branch, Office of Communications and Public Liaison, National Institutes of Health, Department of Health and Human Services. For editorial policies, email editor or phone (301) 496-2125.

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NIH National Institutes of Health
Turning Discovery Into Health

Nagler

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“Researchers, clinicians, we’re pretty well-equipped to negotiate this...My concern has always been about the public and the public’s ability to reconcile seemingly conflicting information,” she explained.

She defined conflicts in health information in a few ways, including “messages that are providing information about the same behavior, resulting in two distinct outcomes.”

Several factors can account for the disputes, Nagler explained. Distinct study design or variations in measurement are two examples. “Early cohort studies pointed to potential benefits of antioxidants and certain individual vitamins, but in the later, randomized control trials, results “didn’t hold up. That’s another place where there could seem to be a shift in findings...”

“This is just the very nature of scientific discovery,” she said, “and we’re seeing that play out in the covid context right now. As research—as knowledge—advances, there is going to be that sort of two-steps-forward/one-step-back approach. And we can wind up with situations where there are legitimately opposing effects.”

Generally, she noted, public understanding of scientific research is limited, a fact that the National Science Foundation has been documenting for years. A large percentage of Americans don’t know what scientific study is.

“We’re seeing a lot of these gaps play out now with Covid-19, with limited research literacy among the public and variations in people’s understanding of risk,” Nagler said.

In addition, she noted, “news coverage historically has omitted a lot of the methodological and contextual information that people would need to make sense of these findings and understand why there could be shifts and seemingly inconsistent results.”

So the media sends mixed messages and the public might be confused. Would people’s behavior reflect this?

Over the years, “there were a lot of assumptions of adverse media effects—this belief that the media was disseminating all of this conflicting information and it was having all sorts of deleterious effects,” said Nagler, who took issue with the assumptions, mainly because she couldn’t find any

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—DR. REBEKAH NAGLER

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empirical evidence linking media exposure to the reported outcomes. She and colleagues set out to provide data on how people are exposed to messages and whether behavior changes as a result.

One key finding: Conflicting nutrition messages delivered by television were perceived differently than messages in print media. TV was associated with greater confusion and, in turn, more distrust in dietary recommendations. Researchers also saw some evidence of reduced health behaviors linked to the confusion people felt, with markedly lower levels of fruit and vegetable consumption, for example.

Nagler’s group also looked at messages involving e-cigarettes, the HPV vaccine as well as guidelines for mammography and screening for prostate cancer. The researchers considered accuracy of the media reports as well. Many 2009 broadcasts of mammography guidelines, for instance, contained mistakes or erroneous reporting.

Timing of the research could prove significant too, Nagler found. Debates surrounding the Affordable Care Act coincided with media events about shifts in cancer screening recommendations from major professional organizations.

“So what we did—through systematically analyzing media content—was ask to what extent did discourse around the controversy evolve?” Nagler explained. “How much explicit

mention of conflict and controversy is there? How much attention was paid to risks and benefits, on balance?”

Researchers were able to connect some subsequent actions to respondents’ exposure to warring medical messages, particularly in a study about mammography screening.

But, specific behavior changes aside, why does it matter whether people take note of a couple of conflicting health stories? What’s the real harm?

Nagler worries about what she termed the “carryover or spillover” result. She described a worst case “cumulative, across-topic, across-source meta effect” on someone exposed to volumes of conflicting or controversial media content over time.

“It could ultimately systematically undermine their trust in science at large, but specifically in public health recommendations,” she said.

As an example, she referred to a 2014 study in which people who were exposed to conflicting reports about wine, fish and coffee were shown to be less inclined to eat fruits and vegetables, which have never been in dispute as healthy.

In the Q&A period, an attendee asked about the potential impact of health



Dr. Abby Ershow (l) of the Office of Dietary Supplements introduces Nagler, who has been looking at how health messages are received by the public.



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messages delivered via Twitter, Facebook and other social media platforms.

“What’s unique about social media, of course, is the ability to share and disseminate,” Nagler responded. “And a lot of the concern is about misinformation...How quickly and easily we could share information is super problematic right now.”

What about getting messages directly from the horse’s mouth, so to speak? Would surveying scientists with health-related questions and sharing results with the public help solve some of the contradictions presented by media?

“I don’t know if it would necessarily solve the problem, but it might at least help get an upstream factor where you know who is doing the actual message creation and development,” Nagler concluded. “To what extent do scientists feel that it is their responsibility to help communicate their results? I think the move towards open communication and public engagement in the last couple years is really positive. Journalists often struggle to get researchers to call them back to serve as sources and help talk things through for the public. I would like to think that could be a potential solution or part of a solution.” **R**

STARTS THIS FALL

Zenk Selected as Next NINR Director

On July 1, NIH director Dr. Francis Collins announced that he selected Dr. Shannon Zenk as the next director of the National Institute of Nursing Research.

A registered nurse and leading nurse researcher, Zenk is currently nursing collegiate professor in the department of population health nursing science at the University of Illinois at Chicago (UIC) College of Nursing and a fellow at the UIC



Dr. Shannon Zenk

PHOTO: UNIVERSITY OF ILLINOIS AT CHICAGO

Institute for Health Research and Policy. She is expected to begin her new role as NINR director in early fall.

“Dr. Zenk’s diverse and original research experience paired with her expertise as a nurse educator make her an ideal choice to lead NIH’s efforts in nursing science,” said Collins.

As NINR director, Zenk will oversee NINR’s science that seeks to improve the lives of individuals and families living with illness and to develop personalized strategies to maximize health and well-being at all stages of life and across diverse populations and settings.

Zenk’s research focuses on social inequities and health with a goal of identifying effective, multi-level approaches to improve health and eliminate racial/ethnic and socioeconomic health disparities.

Her research portfolio also includes NIH-supported work into urban food environments, community health solutions and veterans’ health.

Through pioneering research on the built environment and food deserts, Zenk and her colleagues helped bring national attention to the problem of inadequate access to healthful foods in low-income and black neighborhoods.

Zenk was elected as a fellow of the American Academy of Nursing in 2013 and was inducted into the International Nurse Researchers Hall of Fame in 2019. She has spent time as a visiting scholar in Rwanda and Australia.

She earned her bachelor’s in nursing, *magna cum laude*, from Illinois Wesleyan University; her master’s degrees in public health nursing and community health sciences from UIC; and her doctorate in health behavior and health education from the University of Michigan.

Upon Zenk’s arrival at NIH, current NINR acting director Dr. Tara Schwetz will continue in her role as NIH associate deputy director.

Harris

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bringing us closer to better treatments.

One such investigator, Dr. James C. Harris, director, Developmental Neuropsychiatry Clinic and professor at Johns Hopkins University, has devoted more than 30 years to studying neurogenetic syndromes, particularly Lesch-Nyhan syndrome (LNS), in which patients are prone to self-injury.

Harris, who spoke at a June 3 virtual Clinical Center Grand Rounds, showed graphic images of patients' self-mutilation: a missing finger and lip disfigurement from self-biting and an eye injury from self-hitting. These patients had classic LNS, a genetic disorder also characterized by other aggressive behaviors, dystonic movement disorder and intellectual disability.

This rare syndrome, first described in 1964 by Dr. Michael Lesch, then a medical student, and his mentor Dr. William Nyhan, stems from a deficiency of an enzyme that, 3 years later, NIH's Dr. Jay Seegmiller would



Objectives

- Review the Neurobiology of Self-Injurious Behavior in Lesch Nyhan Syndrome
- Examine the Spectrum of HGprt Deficiency Utilizing Clinical Assessment, Neuroimaging, Neuropsychological, &

Harris speaks virtually to an NIH audience at Grand Rounds.

said Harris. "These children are particularly sensitive to attention to their disruptive behavior."

Not all LNS patients injure themselves. Classic cases with less than 1 percent HGprt enzyme present with self-injury, but there are variants. Patients who have 3-5 percent enzyme tend to have dystonia and other neurological symptoms but don't self-injure. Other patients who have closer to 20 percent enzyme also don't self-injure; they tend

[Nyhan's] description set us off to try to understand what those deficits were."

Over the years, Harris and his colleagues' NIH-funded research has delved into the spectrum of HGprt enzyme deficiency, measuring metabolites and studying the underlying neurobiology. Their numerous studies sought to gauge motor, cognitive,

to have some motor clumsiness and mild to no dystonia. All of them have hyperuricemia, but treating it has no effect on the self-injury.

"Overall, the variants contribute a great deal because they allow us to look at an extended phenotype," said Harris. "[LNS variants also allow us] to carry out cognitive and behavioral measures across the full spectrum, keeping in mind that self-injury is one symptom that's apparent only in classic cases with essentially no enzyme."

In a recent study with 17 LNS patients compared with healthy subjects, Harris and colleagues found discrepancies in white matter, areas deep in the brain teeming with nerve fibers and encased in a protective myelin sheath that affects motor, sensory and cognitive function.

"I think this is particularly interesting because no one has looked carefully at white

• • •
"It was an interesting idea that a behavior could designate a newly described genetic metabolic syndrome, and [Nyhan's] description set us off to try to understand what those deficits were."

-DR. JAMES C. HARRIS

identify as HGprt. The less enzyme present, the more severe the patient's symptoms.

The amount of HGprt deficiency is based on the type of mutation—there are hundreds of possible ones—of a single X-linked gene. That gene, HPRT1, was first sequenced in the 1980s, around the time Harris came on the scene to study LNS.

Nyhan had described LNS as involving structural deficits in the central nervous system with the characteristic behavioral phenotype of self-injurious behavior. Further research would reveal the syndrome is an X-linked metabolic disorder: the enzyme deficiency causes hyperuricemia—excess uric acid in the blood.

"It was an interesting idea that a behavior could designate a newly described genetic metabolic syndrome," said Harris, "and

linguistic and social abnormalities in LNS patients. He continues to use the latest imaging technologies to analyze brain structure and chemistry, looking at pathways from genes to self-injury.

In classic LNS cases, patients often wear arm restraints to protect against self-injury, though some can communicate when they feel safe enough to loosen them. Harris told the story of a young boy named John who told his caregivers when he felt safe enough to have his restraints released. On one occasion, Harris said, while a caregiver was transferring John from bed to his wheelchair, his hand inadvertently hit his caregiver in the face.

"The caregiver continued as if nothing had happened because if he responded, he'd reinforce the behavior and it would persist,"



Dr. Maryland Pao, clinical director, NIMH Intramural Research Program, introduces Harris, whom she met as a medical student at Johns Hopkins. "He and his wife Cathy DeAngelis became my academic parents and shepherded my early career at Hopkins, for which I am eternally grateful," she said.

matter in LNS before,” said Harris.

Using diffusion tensor imaging, they are finding markedly less white matter in the brains of LNS patients, and the white matter is abnormal.

“Strikingly, the classic Lesch-Nyhan cases are consistently lower in their cognitive capacity on [verbal learning and recognition] tests than the variants and both are quite different from the normal controls,” he said.

Over the years, treatments for LNS have included symptom management, protective equipment along with psychiatric, occupational and speech therapy interventions. Among the pharmacotherapy options, researchers continue to focus on dopamine (D1) receptor antagonists, which may show benefit in treating dystonia and self-injury, said Harris.

A recent, promising clinical trial using the D1 drug ecopipam produced significantly less frequent and severe self-injury but the trial was canceled due to side effects, said Harris, noting that doses may need tweaking in subsequent studies if the drug can again be made available for further study.

“We’re hoping this type of work can be continued,” said Harris, “because the D1 antagonist is the only drug treatment we’ve seen that’s actually been demonstrated to have an effect in a controlled study.”

Another promising treatment, particularly in children with LNS, is a metabolic precursor using the dietary supplement S-adenosyl-methionine (SAME). Harris is encouraged by the neurobehavioral improvement in SAME trials, adding that the treatment remains a work in progress that requires refinement. Benefit is reported in approximately 30 percent of adult cases.

As Harris and colleagues fine-tune their understanding of the neurobiological pathways of LNS, another approach—targeted deep-brain stimulation—has helped improve, and in some cases eliminated, self-injurious behavior. He showed a video clip of a patient self-biting, spitting up food and hitting his caretaker at baseline. Later, after deep-brain stimulation, the patient is calm, amicably interacting with others, with no sign of self-injury.

Building on decades of research, new studies renew hope of finding more effective, sustainable treatments for LNS and other developmental neuropsychiatric conditions. **B**



HHS Deputy Hargan Returns to Give Blood

On July 1, HHS Deputy Secretary Eric Hargan and his chief of staff Will Brady donated blood in support of Clinical Center patients. This is a continuing effort by Hargan to bring attention to the importance of blood donation during the Covid-19 pandemic. He wants to highlight that donating blood is safe and encourage healthy individuals to help with blood, platelet and convalescent plasma donations. At top are (from l) Dr. Kamille West, chief of the department of transfusion medicine’s blood services section; Hal Wilkins, donor resources supervisor; Hargan; Brady; and Kathy Robinson, donor resources specialist. At right center, Hargan is taken care of by Ahmed Cham; Brady (bottom) is seen to by Beisha “Belle” Zhu. Hargan had visited the NIH Blood Bank on Mar. 24, joined by his wife, to donate blood and make a video on the importance of blood donation.



PHOTOS: CHIA-CHI CHARLIE CHANG



Fagerlin

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societal unrest and a pandemic, Richard Fagerlin, founder and president of Peak Solutions, gave the third talk in the Deputy Director for Management Seminar Series on June 4.

Although his talk was scheduled long before trust was elevated to a crucial national concern—Do we trust the police? Do we trust vaccines?—Fagerlin acknowledged the weight of the moment.

“The times we’re in right now make trust more important than ever before,” he said. “This presentation is absolutely just in time.”

For the last 20 years, the Edelman public relations firm has compiled a Global Trust Report, said Fagerlin. In 2020, its focus is competence and ethics.

“No organizations were found both competent and ethical in 2020,” he said. “Trust is at an all-time low in the systems they examined.”

But the three most trusted occupations in America this year are doctor, scientist and national health official.

“That’s powerful,” said Fagerlin, “because every one of you fits. You are the most trusted people on the planet. You have been placed in the highest position, which has never been the case in the history of time... The whole world’s eyes are upon you.”

But it’s easy to slip when, given any set of circumstances—say, the importance of wearing masks in public—30-40 percent of the public will interpret the same set of facts totally differently.

“These are unprecedented times,” said Fagerlin. “We’re all tired of hearing about it,

but it’s true. These are heavy, scary, difficult times, but historic times, too. Mostly these are revealing times. We show more of who we are under pressure. Pressure makes us more of who we already were.”

With our beliefs and principles put daily to the test, Fagerlin suggests examining the polarities and tensions they reveal.

For example, we all want a boss who is clear. But we also want flexibility.

“There’s a tension between those two values,” said Fagerlin. “Each one is the downside of the other.”

But just as breathing requires both inhaling and exhaling—unless you want

negotiate obstacles, often by accruing trust due to having extended it to others in the past.

Fagerlin says workplace culture is “the sum of what you permit and what you promote.” The best cultures emphasize the latter, which tends to be more positive than a set of strictures and thou-shalt-nots.

Two lies work against a culture of trust, he said: Trust is earned over time, and trust takes a lifetime to earn, but only a second to lose.

Throw away the scorecard, urged Fagerlin. When mistrust emerges between two parties, both often think they’ve gone halfway to meet the other. “It’s the first step past halfway that impresses me the most,” he said.

“Trust isn’t what you earn, it’s something you give. If you don’t give it, you’ll never get it.”

Fagerlin isn’t calling for blind trust or ignorance; there are people who will take advantage of you, but the percentage is small, and the gains of trusting far outweigh the occasional downside, he argued.



“Trust isn’t what you earn, it’s something you give. If you don’t give it, you’ll never get it.”

—RICHARD FAGERLIN



to suffocate—there needs to be a balance between the two.

Another example: Flattening the curve by staying home vs. killing the economy.

“The point of tension isn’t deciding what’s right or wrong, but in admitting what the factors are—safety is paramount in this instance—and learning to manage them,” Fagerlin suggests. “The goal is not to solve a problem, but to manage tensions.”

This often involves abandoning the either/or mindset and welcoming both/and, he said. There is an upside to tension, and the best leaders know better than to resolve all of it. Respect, empathy and an open mind are a leader’s best allies in tight situations.

Leaders, by the way, are not necessarily the experts, or the most senior people. Rather they are problem-solvers who can

Trust is a stool with three legs, he posited: integrity, competence and compassion.

“Integrity is more than honesty,” he explained. “It comes from the same word as integer, or whole number. It’s a wholeness, a consistency of self.”

Competency, he said, is the ability to acquire knowledge, but more crucially, “to be able to broker that knowledge to other people.”

Compassion, he admitted, “is the most difficult. It requires a pure understanding of where people are coming from. You’ve got to be able to rejoice when people are rejoicing and grieve when they are grieving.

“If you have all three of these characteristics, you have trust.”

Interestingly, whichever of the stool legs is most important to you is likely to be the

one you most unfairly judge others by, he said.

“We tend to overvalue what’s important to us,” Fagerlin noted. “Remember, you can inhale too much and end up out of balance.”

He concluded with three suggestions for getting past the halfway point in building a relationship of trust.

- “Everyone needs CPA,” he declared: I cause...I participate...I allow. “This is the coat of arms of our various cultures. We need to take ownership.”

- Always assume positive intent. “I judge myself on my intentions. But I judge others on their actions...Take the risk to assume a positive intention.”

- Be offensive, or willing to offend others. Fagerlin admits that feelings of offense are at an all-time high and cautioned against being a bully. He emphasized “candor with care” in order to be real, authentic and vulnerable. “As the saying goes, wounds from a brother are better than a kiss from an enemy.”

He touted the model of servant leadership: “Lift up others so they can be great. Do the right thing. Ask every day, ‘What’s needed from me right now?’”

And have the humility to forgive others when things go awry. “Choose courage over comfort in taking the first step toward reconciliation.”

During a brief Q&A moderated by NIH deputy director for management Dr. Alfred Johnson—who issued Fagerlin a standing invitation to visit NIH once travel restrictions abate—Fagerlin acknowledged that some employees must cope with malignant narcissism in bosses.

“Don’t let people live rent-free in your brain,” he counseled. “Don’t let them take more energy than they deserve.” He also pointed out that sometimes “there are necessary endings.”

Two final nuggets: clear expectations coupled with immediate and regular feedback are the most motivating factors in the workplace. And when change comes, only three people like it—if they’re in charge, if they implement it, or if they benefit by it.

“It sucks for everyone else!” he said.

The full lecture is available at <https://videocast.nih.gov/watch=35467>. 

Long-Acting Injectable Form of HIV Prevention Outperforms Daily Pill

A pre-exposure prophylaxis (PrEP) regimen containing an investigational long-acting form of the HIV drug cabotegravir injected once every 8 weeks was more effective than daily oral Truvada at preventing HIV acquisition among cisgender men who have sex with men and transgender women who have sex with men in a clinical trial sponsored by NIH.

While both methods were highly effective for HIV prevention in the study population, the final data analysis indicated that cabotegravir had a superior protective effect. Findings from the study, called HPTN 083, were to be discussed during the 23rd International AIDS Conference.

The only currently licensed PrEP medications—daily oral pills containing the HIV drugs tenofovir and emtricitabine—are highly effective at preventing HIV when taken as prescribed. However, taking a pill daily can be challenging. A long-acting form of PrEP could offer a less frequent, more discreet option that may be more desirable for some people. HPTN 083 and an ongoing companion study called HPTN 084, which is evaluating long-acting injectable cabotegravir for HIV prevention in cisgender women in sub-Saharan Africa, are sponsored by NIAID.

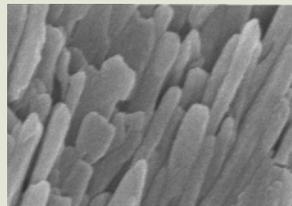
In May 2020, a review of HPTN 083 data indicated a high level of efficacy for long-acting injectable cabotegravir among cisgender men and transgender women who have sex with men. The current results are based on a more extensive analysis of interim data from 4,566 study participants.

Overall, the rate of HIV acquisition in the participants was low. Among the 52 participants who acquired HIV, 13 were in the study group who received the cabotegravir-based PrEP regimen plus placebo daily oral tablets, and 39 were in the group who received daily oral Truvada plus placebo injections. Detailed analysis of these data indicated that the superior efficacy of cabotegravir was statistically significant.

Both products were safe and generally well-tolerated. Participants in the cabotegravir group were more likely to experience fever and pain or tenderness at the injection site compared to those in the Truvada group, who received placebo injections. Those in the Truvada group were more likely to report nausea.

Complexity of Tooth Enamel Revealed at Atomic Level

Scientists used a combination of advanced microscopy and chemical detection techniques to uncover the structural makeup of human tooth enamel at unprecedented atomic resolution, revealing lattice patterns and unexpected irregularities. The findings could lead to a better understanding of how tooth decay develops and might be prevented. The research was supported by NIDCR and findings appeared in *Nature*.



Enamel is made up of tightly bunched, oblong crystals that are about 1,000 times smaller in width than a human hair.

IMAGE: KAREN DEROCHE, NORTHWESTERN UNIVERSITY

“This work provides much more detailed information about the atomic makeup of enamel than we previously knew,” said Dr. Jason Wan, a program officer at NIDCR. “These findings can broaden our thinking and approach to strengthening teeth against mechanical forces, as well as repairing damage due to erosion and decay.”

Your teeth are remarkably resilient, despite enduring the stress and strain of biting, chewing and eating for a lifetime. Enamel—the hardest substance in the human body—is largely responsible for this endurance. Its high mineral content gives it strength. Enamel forms the outer covering of teeth and helps prevent tooth decay, or caries.

To survey enamel at the tiniest scales, researchers use microscopy methods such as scanning transmission electron microscopy (STEM), which directs a beam of electrons through a material to map its atomic makeup.

STEM studies have shown that at the nanoscale, enamel comprises tightly bunched oblong crystals that are about 1,000 times smaller in width than a human hair. These tiny crystallites are made mostly of a calcium- and phosphate-based mineral called hydroxylapatite. STEM studies coupled with chemical detection techniques had hinted at the presence of much smaller amounts of other chemical elements, but enamel’s vulnerability to damage from high-energy electron beams prevented a more thorough analysis at the necessary level of resolution.

“Human enamel is much more chemically complex than we thought,” said co-first author Dr. Paul Smeets, a research associate at Northwestern University. The findings could lead to new approaches to toughen enamel and prevent or reverse cavity formation.



A long-acting form of cabotegravir injected was more effective than daily oral Truvada.

NINDS's Kehne Retires After 35 Years in Neuroscience

BY SHANNON E. GARNETT

For 35 years, Dr. John Kehne, a program director in NINDS's Division of Translational Research, has built a career in neuroscience—primarily focused on discovery and development of new drugs for treating central nervous system (CNS) disorders. He officially retired on June 30.

"I have had a very satisfying career in neuroscience, and feel very gratified that at NINDS I have helped position the Epilepsy Therapy Screening Program [ETSP] for further success, helped build a new screening program for finding non-addicting analgesics and recruited great teams to maximize future success," said Kehne. "I won't leave neuroscience, but I have what seems like several lifetimes of interests and activities I would like to pursue."

Raised by parents who valued broad-based education and stressed the importance of science to their 9 children, Kehne developed an early appreciation for science and had a particular fondness for astronomy. In fact, he might have pursued a career in astronomy if Amherst College had not established the first neuroscience undergraduate program in the United States during his sophomore year. After taking a "fascinating" psychopharmacology course, Kehne became one of the nation's first undergraduate neuroscience majors.

"Bottom line, I still loved astronomy but, to quote the poet Robert Frost, it would be the 'road not taken' as neuroscience and psychopharmacology would form my career's trajectory," Kehne said.

He earned his bachelor of arts degree in neuroscience from Amherst in 1976 and pursued doctoral training in psychology with an emphasis in psychopharmacology at the University of Massachusetts, earning his Ph.D. in 1983. Kehne completed a postdoctoral fellowship in biological psychiatry in 1985 at Yale University School of Medicine, which led to an associate research scientist position.

Kehne later became a discovery scientist in the pharmacology department at Merrell Dow Pharmaceuticals in Cincinnati. While there, he provided *in vivo* pharmacology support for a wide variety of projects that targeted various psychiatric and neurological disorders.

In 1996, Kehne joined Neurogen—a CNS biotech company in Branford, Conn.—where he advanced to the level of executive director of pharmacology. At Neurogen, he also served as the biology co-leader of a team that identified and



Dr. John Kehne

characterized novel CRF-1 receptor antagonists for the treatment of depression, anxiety and stress-related disorders, helping to successfully secure a multi-year collaboration with a large pharmaceutical company.

Upon leaving Neurogen, Kehne became an independent consultant working with biotech companies to advance compounds through discovery and development.

In 2012, he joined the NINDS Division of Translational Research (DTR) as a scientific project manager and acting director of the Anticonvulsant Screening Program (now ETSP)—a preclinical platform for identifying potential new drug treatments for epilepsy. He later became a DTR program director with interests in preclinical pharmacology, animal models and preclinical neurotherapeutic development, and head of ETSP.

"I was particularly excited by the specific challenge posed to me of taking a longstanding, highly successful preclinical epilepsy screening program to the next level to address critical unmet medical needs in epilepsy," said Kehne.

Most recently, he contributed to the conception and development of a new NINDS preclinical program for identifying non-addicting analgesic alternatives to opiates, as part of the NIH Helping to End Addiction Long-term (HEAL) Initiative to address the nation's opioid crisis. According to Kehne, ETSP served as a prototype for this new program.

In retirement, Kehne plans to pursue his many hobbies and interests including several outdoor activities such as gardening, hiking and canoeing, as well as woodworking, music and rekindling his passion for astronomy.

"Throughout my career, I have been fortunate to be a member of many talented teams that have tackled immensely challenging problems," he said. "To quote Michael Jordan, 'Talent wins games, but teamwork and intelligence win championships.' So, I truly thank all of those team members with whom I have had the privilege of working and I applaud my NINDS colleagues for the tremendous progress made in advancing an array of new translational programs to facilitate therapy development."



Dr. James Schmitt

include staff physician and senior staff physician in OMS.

As medical director, he established operational priorities for OMS and developed, implemented and adjusted work-related medical and counseling services to meet the evolving needs of the NIH workforce.

Schmitt is responsible for establishing the first postexposure chemoprophylaxis program for HIV-1 exposures in the nation. He also developed the first standardized approach for evaluating and treating workers for potential exposures to B virus. Other career highlights include designing the medical portion of the NIH biological surety program and revamping OMS operations to provide support for the NIH community during the Covid-19 pandemic.

Upon retirement, Schmitt plans to travel nationally and internationally (when the pandemic subsides), spend time with grandkids and extended family and complete a long list of woodworking projects and consulting. He says he will miss "patient-care responsibilities, daily interactions with the amazing OMS and NIH staff, an incredible variety of clinical and administrative challenges, and being involved in supporting the NIH mission."

NHLBI's Hewitt Mourned

Keith Hewitt, former head of the information services section at the National Heart, Lung and Blood Institute, died of natural causes at his home in Sao Jose do Calçado, Brazil. He was 80 years old.

Hewitt began his federal career as a Peace Corps volunteer in Brazil after graduating from the University of Wisconsin in 1964. He met and married his wife Ketta in Brazil. Upon returning to the U.S., he was named chief of the Education Branch in the Peace Corps/Action Office of Volunteer Placement.

He then worked with the National Institute on Alcohol Abuse and Alcoholism for several years, where he directed youth programs. He organized the first National Conference on Alcohol and Youth at Notre Dame University. With students and faculty/staff from colleges around the U.S., the conference was the first to identify and evaluate programs designed to reduce alcohol abuse among college students. The program manual he wrote based on conference deliberations, *Beer Is a Four-Letter Word*, was used on college campuses for several years.

In 1985, he joined NHLBI, where he initiated extensive collaborations with state health departments.



Keith Hewitt

His groundwork resulted in annual conferences with state health department officials responsible for cardiovascular risk reduction. Hewitt worked closely with the members of NHLBI's National High Blood Pressure Education Program, National Cholesterol Education Program and National Asthma Education Program to develop risk-reduction education programs. After leaving NHLBI, he continued to work with NIH, helping to establish NICHD's National Maternal and Child Health Education program.

Hewitt's colleagues found that working with him was plain fun. Whether planning a national conference or coordinating community outreach strategies, he infused energy and purpose into what others may have seen as an impossible project schedule, driven perhaps by his rigorous training for the marathons he ran in the U.S. and abroad. Over the years, he worked with hundreds of people at NIH and state health departments and, remarkably, he kept in touch with most of them. His instincts were the perfect fit for his role of promoting and diffusing NIH science: welcome friends, build coalitions, grow the network, improve public health.

Hewitt is survived by his wife Ketta and sons Frederico and Erik who live in Brazil, and his daughter Yedda, who lives in Virginia.

Former DRG Director and NIH Scientist Wife Remembered

BY DON LUCKETT

A remarkable couple who devoted most of their lives to public service and health at NIH recently passed away. At age 91, they both succumbed to Covid-19. Dr. Jerome "Jerry" Green died on Apr. 26 and Dr. Marie Röder Green died on May 10. But Jerry and Marie should be remembered as a scientific power couple.

Jerry retired as director of the Division of Research Grants (now the Center for Scientific Review) in 1995, after 40 years of service at DRG, NHLBI and in the Commissioned Corps. Marie retired as an NHLBI program officer after many years of federal service.

Thousands of scientists across the country still benefit from Jerry's efforts to advance NIH extramural research programs.

While at DRG, he championed the First Independent Research Support and Transition (FIRST) award, which supports newly independent investigators, and the Method to Extend Research In Time (MERIT) award, which provides long-term support to investigators who demonstrate remarkable ability and productivity.

Marie was a trailblazer at a time when few females worked at the bench. In 1956, she joined an intramural lab at what is now NIAMS. After she and Jerry started their family in California, she returned to the bench at what is now Case Western Reserve University in Cleveland.

Moving back to D.C., she joined the Armed Forces



Dr. Marie Röder Green and Dr. Jerome "Jerry" Green should be remembered as a scientific power couple.

Institute of Pathology in Washington, D.C. Marie eventually returned to NIAMS under a fellowship in its Laboratory of Biochemistry and Metabolism. She later moved to NCI, where she primarily studied breast cancer in its Laboratory of Molecular Carcinogenesis. Marie then joined NHLBI in 1988, after a couple of years away from NIH.

According to their daughter, Karen Green, they encouraged each other in nightly discussions of science and work at the dinner table. Some of those discussions likely focused on Marie's effort to advance research on carcinogens in cosmetics and to get the FDA to act after she discovered that a stain called Stanzel could detect possible

carcinogens in lipstick. Finally, after she published a study in 1980—"Mutagenicity of Some Lipsticks and Their Dyes"—in the *Journal of the National Cancer Institute* and other researchers weighed in, the FDA banned the use of Orange No. 17 dye in cosmetics 3 years later.

Jerry and Marie's love affair with each other and science began when they met in freshman biology class at Brooklyn College. After Marie earned a master's in zoology at the University of Wisconsin, she married Jerry and joined him at Albany Medical School, where he earned his M.D. and she earned her Ph.D. in pathology.

In 1955, Jerry joined what is now NHLBI and the Commissioned Corps, which sent him to the San Francisco PHS Hospital for his residency. While there, he also served as a special research fellow

at the Cardiovascular Research Institute at the University of California, San Francisco. He and his family then moved to Ohio, where he was a senior research fellow and clinical investigator at the Cleveland Clinic.

Jerry returned to NHLBI in 1965 to help lead its extramural programs and eventually became its director of extramural affairs. His accomplishments advancing NHLBI's extramural programs were recognized when NIH named him DRG director in 1986.

When Jerry retired in 1995, he was a rear admiral and assistant surgeon general in the PHS, conferred by Surgeon General C. Everett Koop. He also garnered multiple awards

in his career, including the Assistant Secretary for Health's Award for Exceptional Achievement "for outstanding leadership in effecting changes in NIH extramural program activities."

Jerry and Marie both came from families that gratefully found homes in the U.S. after fleeing persecution in Europe. As a result, "they were very big social justice people," said Karen. "They gave to a lot of causes like the Southern Poverty Law Center and the ACLU, and Doctors Without Borders."

The concern Jerry had for others radiated into his work life. "He raised the bar in DRG," said Barbara Williams, his former secretary and long-time friend.

• • •
Both Greens came from families that gratefully found homes in the U.S. after fleeing persecution in Europe. As a result, Jerry and Marie "were very big social justice people."
• • •

"He brought a whole new level of respect for everyone who worked there...and he gave me the confidence and tools to succeed when I moved to the NIH Executive Secretariat."

The admiration he earned also endured. Anne Stroh, a former DRG and NHLBI human resources specialist, explained: "After he retired, several of us routinely had lunch with Dr. Green...This continued in more recent years with visits with him and his wife." Stroh treasured these conversations, which sparkled with humor and intelligence even in later years.

Condolences and remembrances would be appreciated via jerryandmariegreen@gmail.com. **R**

CIT Produces Ear Savers, Nasal Swabs for NIH'ers

BY SARAH FICHTER, ROBERT WAXMAN

As the Covid-19 global pandemic continues, testing and protection for health care workers and support staff remain critical in responding to the crisis. To support these efforts, the Center for Information Technology's signal processing and instrumentation section (SPIS)—a central NIH bioengineering resource that provides custom engineering solutions and in-house fabrication for NIH Intramural Research Program projects—turned their experience in rapid prototyping, novel instrumentation design and software development toward devising tools and equipment that could help.

Two results of their creative work are the design and production of ear savers that help alleviate discomfort from wearing disposable face masks and in-house production and evaluation of 3-D-printed nasal swabs to use for Covid-19 testing.

Face Mask Ear Savers

Ear savers may not seem like important equipment, but they can make a difference in comfort and safety for health care workers. Clinical Center staff—in particular nurses working 8-hour shifts or longer—are required to wear surgical or disposable face masks throughout their shifts for protection. Friction from mask straps can cause irritation and even abrasions to ears when worn for long periods over consecutive days, which can make nurses' already difficult work more challenging. To provide more comfort and safety to medical staff, the SPIS team created ear saver straps designed to relieve painful chafing and irritation from prolonged wear of disposable face masks.

SPIS set out to design a reusable, quickly produced and cost-effective ear saver device that could be cleaned with common supplies. While the most common ear saver designs include features that require fabrication using widely available 3-D-printing technologies, the team focused on designs that could be laser-cut from acrylic sheets.

This approach offered several advantages: bulk acrylic sheet costs less than 3-D printer materials; using this material means the ear saver can be more easily disinfected; and laser cutting offers a much faster production rate than 3-D printing.

The SPIS team chose a two-dimensional design that included multiple hooks for size adjustment. When testing the available acrylic to find something that could conform to the back of the head without being uncomfortable or too brittle and prone to breaking, the team discovered that acrylic left over from a previous IRP scientific collaboration performed the best due to its thickness. The material was flexible enough to improve comfort significantly but still durable enough to withstand the tension of mask straps.

Due to the limited on-site staff available to help evaluate the fit and comfort of the ear saver, an SPIS engineer asked his wife to try the device at

home. This revealed a problem they had not previously considered: the hook configuration of the original design could get caught in long hair. To help prevent this issue, the team developed a new design with an alternate hook shape and a long rectangular back. They called the new design the Tsunami Ear Saver, named after the shape of the strap hooks. The straps are available in two configurations to accommodate different head sizes. This design allows the strap to conform with the back of the head and eliminates pressure points while the hook design reduces the chance of hair tangles.

Robert Reff, a nurse at the Clinical Center who usually works 12-hour shifts, was an early adopter of the Tsunami Ear Saver and quickly became a fan. "The ear savers work great for me because I no longer have any ear pain after wearing masks for extended periods of time," he says. "The ear saver works great with the combination of the KN95 [mask] and the cloth mask on top because they are both held by the ear saver. Before, they both would sometimes slide off my ear because two masks around my ears created a lot of pressure and bent my ears forward and made the masks slide off."

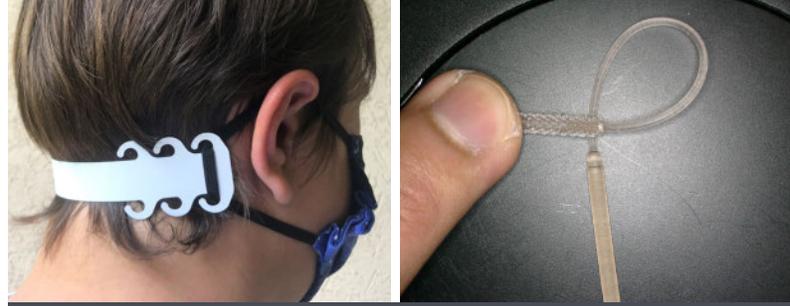
Reff is not alone, as several groups of Clinical Center nurses are interested in the Tsunami Ear Saver and have even asked for different versions of the design. SPIS hopes their device will also prove useful for other NIH employees when they begin to return to physical workspaces and are required to wear masks.

3-D-Printed Nasal Swabs

Testing is key to gathering data that informs responses to the pandemic, and testing can only be done with the appropriate equipment. To help find solutions to covid-related problems like localized shortages of certain medical supplies, the SPIS team started a general knowledge-sharing exchange with its long-time intramural and extramural collaborators.

Aware that Children's National Hospital in Washington, D.C., was concerned about a possible shortage of nasal swabs for testing, the team shared the design of a 3-D-printable nasopharyngeal swab developed by the University of South Florida in collaboration with Formlabs and Northwell Health. Because Children's was not equipped to print the swab in its own labs, the SPIS team offered to work with them in evaluating these new 3-D-printable swabs for potential use at the hospital.

A thorough evaluation and approval of the swabs by hospital staff was especially important because 3-D-printed swabs are distinctly different in size, shape, flexibility and texture from the normal FDA-approved swabs commonly used. This can be a concern for patient comfort, especially in children, and the fact that 3-D-printed swabs look markedly different from normal ones can deter medical staff and patients from using them.



The ear saver device is shown at left; at right is the 3-D printed swab.

To give Children's staff the opportunity to physically handle the swabs and become familiar with the design, the SPIS team printed several dozen swabs and asked the hospital's laboratory pathology and sample collection staff to examine them and provide feedback on how the swabs' physical properties might affect their work with patients.

SPIS was specifically concerned about the safety and durability of the 3-D-printed materials. To assess whether the material might be brittle and prone to breaking, the evaluation included performing mechanical testing to determine conditions under which the swabs might break. This involves twisting and bending the swabs well beyond what would happen in actual patient use to identify any weak points. Children's laboratory personnel were also concerned about possible interactions between testing reagents and the 3-D-printed materials that could affect virological analysis results. Each organization that prints the swabs is encouraged to perform its own evaluations, and SPIS is coordinating with other stakeholders during the testing process.

To be ready for a possible resurgence of the virus this winter, SPIS worked with staff from the Children's National Hospital biomedical engineering team and the Walter Reed National Military Medical Center's 3-D Medical Applications Center on evaluating the swabs and manufacturing requirements, to help develop the required regulatory and process controls, documentation and safety testing needed for consistent and safe production of the swabs. If rapid production of swabs becomes necessary in the future to alleviate shortages, the ongoing collaborative preparations will facilitate NIH swab production.

Confronted by this pandemic, the CIT SPIS team developed practical solutions for frontline health care workers by expanding its collaborative work and quickly reorienting its members' engineering knowledge and experience toward the new problems posed by Covid-19.

"The team's flexibility and creativity in approaching our community's needs is just one of many examples of the larger NIH Intramural Research Program's rapid response to this pandemic," said Dr. Andy Baxevanis, CIT's acting scientific director and director of computational biology for the IRP. "NIH's approach of fostering interdisciplinary, cross-IC technology groups such as the SPIS team allows the IRP to quickly address emerging global health challenges through many different approaches. You never know what solution, big or small, the minds at NIH might think of next, once given the challenge." 