



National Institutes of Health

MULTIPLE 'ACTTS'

NIID Researcher Discusses Outcomes of Covid Antiviral Studies

BY DANA TALESNIK

Researchers knew they had to act fast. Alarmed at the first reports of a quickly spreading new coronavirus in early January 2020, NIAID researchers immediately began planning for clinical trials to test promising therapeutics even before there were known Covid-19 cases in the U.S.

“Our initial focus was getting the vaccine study started but we quickly started planning [a clinical trial for the antiviral remdesivir] as we saw more and more cases,” said Dr.

John Beigel at a Covid-19 Scientific Interest Group virtual lecture earlier this year.

Beigel, associate director for clinical research in NIAID’s Division of Microbiology and Infectious Diseases, has been instrumental in NIH’s research response to respiratory viruses for nearly 20 years. Last year, he led the team implementing the Adaptive Covid-19 Treatment Trial (ACTT), the first large U.S. Covid-19 study launched after the first U.S. patients were identified.

On Jan. 31, 2020, Beigel and colleagues submitted a synopsis of a trial design to the FDA. Three weeks later, the first ACTT site was activated. In less than a year, four phases of ACTT were launched to study the

leading antiviral and anti-inflammatory candidates in hospitalized Covid-19 patients.

The effort required pooling resources and identifying sites of high epidemiology across the country and around the world. Enrollment for ACTT-1 started slowly, then rapidly expanded, mirroring the Covid trajectory across the country, recounted Beigel.

In 58 days, the trial had enrolled 1,062 people at 71 sites across 10 countries. Conducted at sites across the U.S., Europe and Asia, the results from ACTT-1 led to the licensing of the antiviral remdesivir and ACTT-2 supported FDA’s emergency use authorization of the anti-inflammatory baricitnib.

In ACTT-1, participants received



Dr. John Beigel

SEE BEIGEL, PAGE 4



Dr. Mona Hanna-Attisha

Pediatrician Who Uncovered Flint Water Crisis Recounts Experience

BY ERIC BOCK

In the summer of 2015, Dr. Mona Hanna-Attisha was drinking a glass of wine with a high school friend in Flint, Mich. Her pal, a drinking water expert, told her the tap water in Flint wasn’t treated properly and probably contained lead.

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THE VIRTUAL DISCONNECT

Morgan Divulges How to Communicate Better Online

BY DANA TALESNIK

Ever receive a work email with only the words “nice job” and wondered if the sentiment was sincere or sarcastic? Ever ask a question on a Zoom meeting only to become flustered at the deafening silence?

These are common concerns in the virtual world, where our intentions and reactions are easily and frequently misunderstood, explained Nick Morgan, a communication coach, commentator and



Nick Morgan

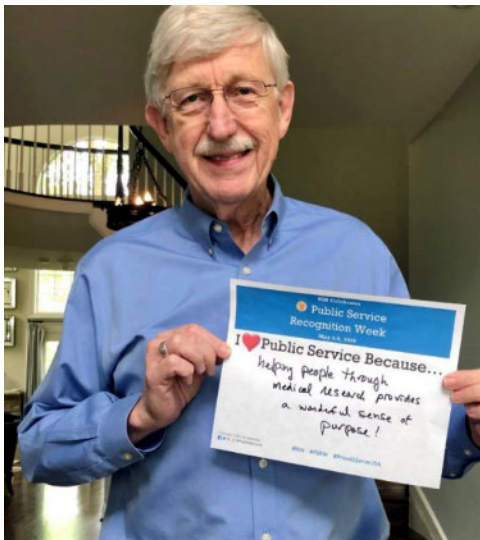
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Astronaut chats from space. See story, p. 9.

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NIH director Dr. Francis Collins shares pride in public service.

NIH Observes Public Service Recognition Week

Each year the President and Congress designate the first full week of May as Public Service Recognition Week (PSRW) to honor those who serve as government employees.

With all of the challenges this past year, now more than ever, the amazing work NIH employees do deserves acknowledgment.

During May 2-8, you have an opportunity to share pride in your public service by participating in NIH's social media campaign for Public Service Recognition Week. Here's how it works:

Take a photo with your completed "I ♥ Public Service Because..." whiteboard template, which can be found on the NIH Office of Human Resources Public Service Recognition Week site at <https://hr.nih.gov/about/events/psrw>.

Post your photo on Facebook or Twitter using the following hashtags: #NIH, #PSRW and #Proud2ServeUSA. The #NIH hashtag allows NIH to find our employees.

If you have any questions about PSRW at NIH or to send your photo to be posted on NIH social media outlets, email NIHPSRW@nih.gov.

FAPAC To Host Panel Discussion on Leadership for AAPI Heritage Month

In observance of Asian American and Pacific Islander Heritage Month, the NIH chapter of the Federal Asian Pacific American Council (FAPAC) will host "Conversations with AAPI Leaders at NIH: Tips on Leadership and Empowering the Next Generation," a panel discussion on Tuesday, May 4 from 3 to 4 p.m. ET, featuring Dr. Noni Byrnes, director of the Center for Scientific Review; Dr. Michael F. Chiang, director of the National Eye Institute; and Dr. Rena D'Souza, director of the National Institute of Dental and Craniofacial Research.



CSR director Dr. Noni Byrnes (l), NEI director Dr. Michael F. Chiang and Dr. Rena D'Souza will be featured in a panel discussion on May 4.

The event will recognize AAPI leaders who have made a significant impact in the field of public health, and provide a platform where they can share insights, leadership tips and vision for the future. Byrnes, Chiang and D'Souza are visible in the AAPI community and beyond; their work and leadership are focused on empowering the next generation of leaders.

NIH principal deputy director Dr. Lawrence Tabak will introduce the panel, which will be moderated by Dr. Christina Liu, chief of the Biomedical Technology Branch in NIGMS's Division of Biophysics, Biomedical Technology & Computational Biosciences.

Live captions will be provided. For additional information or to request reasonable accommodation, email xinzhi.zhang@nih.gov. As May continues, check out the campaign to celebrate AAPI Heritage Month via the Office of Equity, Diversity, and Inclusion website at www.edi.nih.gov/people/sep/aapi/campaigns/aapi-heritage-month-2020.

'INTEGRATING SEX, GENDER INTO BIOMEDICAL RESEARCH'

ORWH Presents 5th Annual Pinn Symposium, May 11-12

NIH's Office of Research on Women's Health will host the virtual 5th annual NIH Vivian W. Pinn Symposium, "Integrating Sex and Gender into Biomedical Research as a Path for Better Science and Innovation," on May 11-12. Held each year during National Women's Health Week (May 9-15, 2021), the symposium honors the first full-time director of ORWH.



Former NIH associate director for research on women's health Dr. Vivian W. Pinn addresses a previous year's symposium.

Attendees of this year's symposium will explore specific strategies for creating bridges and capacity across the scientific enterprise to build a broad-based network of government, nonprofit, academic and business organizations; integrating sex and gender considerations into the research enterprise; and applying a multidimensional perspective to women's health to advance the integration of sex and gender considerations via transdisciplinary approaches and partnerships.

More information, including registration instructions, will be posted at <https://fnih.org/what-we-do/programs/fifth-annual-vivian-pinn-symposium-integrating-sex-and-gender-biomedical>.

NIEHS Donates Freezers for Covid-19 Vaccine Storage

BY KELLY LENOX

On Mar. 16, NIEHS shipped 11 ultracold laboratory-grade freezers to the North Carolina department of health and human services (NC DHHS), thanks to a grassroots project from within the institute's Office of Management.

The donation is the brainchild of three OM employees, who took it on as part of a leadership training program: Andrea Davis, management and program analyst; Kerri Hartung, sustainability coordinator; and Rick Weaver, inventory management specialist. The project took advantage of energy efficiency upgrades that were part of the institute's continued sustainability efforts. As a result, more communities in the state are equipped to receive doses of the Moderna and Pfizer Covid-19 vaccines.

The team did not work alone. "It came to fruition thanks to many helping hands across the institute," said Hartung.

"Many of our rural counties have been relying on dry ice storage because they do not have the required ultracold freezers," noted NIEHS and National Toxicology Program director Dr. Rick Woychik. "This is a fantastic representation of NIEHS as a caring partner in the Covid-19 fight."

According to Kim Jones, inventory management officer, donating federal property is not as simple as hauling it to the nearest willing recipient. She ultimately worked through the NC Federal Surplus Property program and NC DHHS, which picked up the freezers. From there, the state took over.

"To simplify the direct donation process and subsequent distribution, NC DHHS will act as a centralized hub, identifying counties in greatest need and transporting the donated surplus freezers to their end users," Hartung explained.



NIEHS's Rick Weaver (r) and David Mills of North Carolina Emergency Management exemplify federal-state partnership as they move freezers into the waiting truck.

PHOTOS: STEVE MCCAW/NIEHS

NC DHHS will collaborate with other state agencies, such as NC Emergency Management and the Division of Public Health (DPH), to determine which localities will receive freezers.

"The donation of the freezers will lessen the burden of storing the vaccine in a thermal shipper container provided by Pfizer and of having to continue procuring and replenishing dry ice every couple of days," said Dr. Amanda Williford of NC DHHS. She added that adequate and plentiful storage provides a true safety net for storing the Pfizer Covid-19 vaccine. "We [NC DPH] are grateful for this partnership with NIEHS."



Kerri Hartung applauds the teamwork that made donation of the freezers possible.



Eleven ultracold freezers were collected from laboratories and readied for pickup from the NIEHS Net Zero Energy warehouse.

Regarding post-pandemic use of the freezers, Jones noted that they now belong to the state, which can decide how best to use them. Laboratory-grade freezers have potential uses from health care settings to community colleges and other educational and training programs. The NC Emergency Management office picked up the freezers from the NIEHS warehouse, which is itself an exemplary effort in

sustainability, with LEED Platinum certification. "Another example of great teamwork and great leadership!" exclaimed Matthew Burr, head of the Administrative Services and Analysis Branch.

The freezer donation would not have been possible without the help of individuals across NIEHS and beyond: Brian Harris and John Sours of NIH ORF located at NIEHS, Paul Johnson and Steve Novak of NIEHS's Health and Safety Branch, Jones of the Office of Management Administrative Services and Analysis Branch, Corey Morris of the Durham County public health department, Michael Spencer of NIEHS's Division of Intramural Research and Williford of North Carolina's DHHS. **R**



ON THE COVER: Ebenezer Mienza, a respiratory therapist, was the first person at NIH to get vaccinated against Covid-19 on Dec. 22, 2020. Recently, NIH expanded employee vaccine eligibility, as the nation gradually begins to emerge from varying degrees of lockdown. Invitations to schedule a vaccine have now been sent to all Phase 4 staff, most of whom continue to work remotely. If you have an NIH staff ID badge and have not received a vaccine, you can schedule an appointment at NIH. As of Apr. 16, approximately 23,625 staffers have received at least a first dose of a Covid vaccine either at NIH or in their community.

IMAGE: CHIA-CHI CHARLIE CHANG

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 nihreford@nih.gov.

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NIH National Institutes of Health
Turning Discovery Into Health

Beigel

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remdesivir or a placebo for 10 days. The endpoint of the 28-day study was the time to recovery or to improved clinical status. On average, the time to recovery for patients on remdesivir went from 15 days down to 10. The antiviral showed greater efficacy in people with more advanced disease, with the most benefit seen in those patients on oxygen. The study, however, did not demonstrate a benefit to mortality.

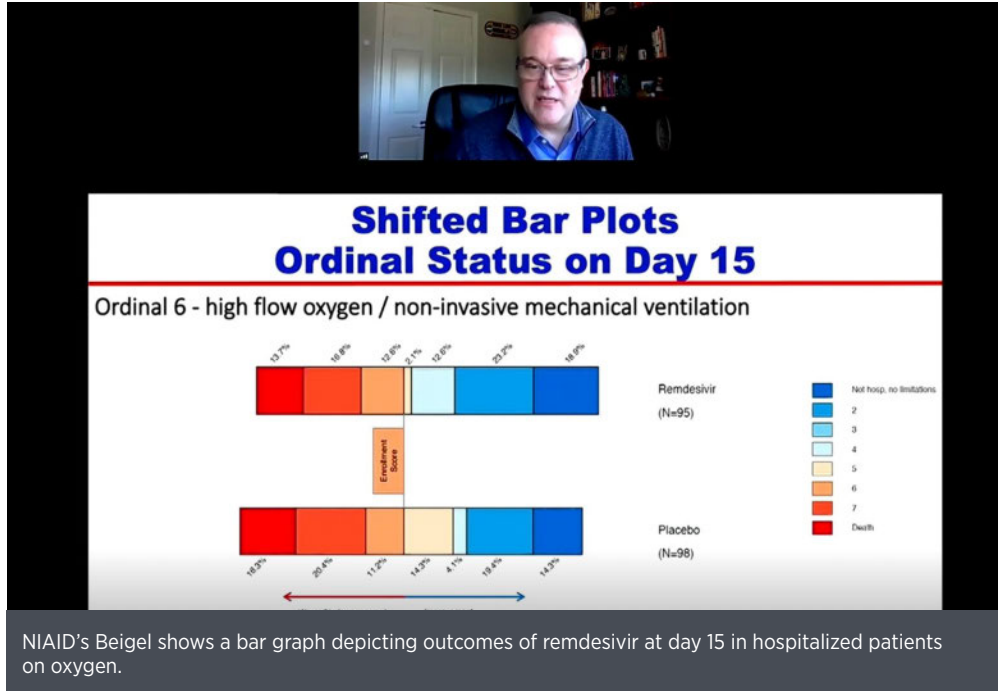
“Is remdesivir effective for treating somebody hospitalized with Covid-19? I think the answer has to be yes—faster recovery, [fewer] days on oxygen, less time on vent—[means fewer] resources that may be strained during a pandemic,” said Beigel. “We see it out in California, when they’re talking about oxygen pipes freezing because there’s so much oxygen flowing through them, because everyone’s on oxygen. If [we] can get people out of the hospital, off oxygen faster, that turns into tangible results.”

The World Health Organization, however, came to different conclusions about remdesivir in its Solidarity trial. The study—involving 12,000 patients hospitalized for Covid-19 at 500 hospitals in 30 countries—tested 4 repurposed antivirals, including remdesivir and hydroxychloroquine. The WHO concluded that none of these antivirals lessened duration of hospital stay or improved mortality rates.



Multiple ACTTs have studied the efficacy of the antiviral remdesivir in hospitalized patients.

PHOTO: MANJURUL/ISTOCK/GETTY



NIAID's Beigel shows a bar graph depicting outcomes of remdesivir at day 15 in hospitalized patients on oxygen.

But there were limitations and biases in this trial, argued Beigel, including lack of a placebo group. “There are no trial results free from uncertainty,” he said. “Bigger trials

★★★

“Is remdesivir effective for treating somebody hospitalized with Covid-19? I think the answer has to be yes—faster recovery, [fewer] days on oxygen, less time on vent—[means fewer] resources that may be strained during a pandemic.”

—DR. JOHN BEIGEL

★★★

are good; bigger trials with more uncertainty are not necessarily better.”

By spring 2020, NIAID launched ACTT-2, enrolling 1,033 hospitalized adults

at 71 sites, to test whether combining remdesivir with the anti-inflammatory baricitnib would improve recovery time and reduce mortality. Investigators chose baricitnib for its safety profile and wide availability worldwide. What’s more, it has potential antiviral effects.

“For ACTT-2, I’d say baricitnib in

addition to remdesivir improves outcomes,” Beigel said. “It improves time to recovery. Those with high- or low-flow oxygen appear to have the largest benefit.”

In ACTT-1, many in the high-oxygen group didn’t significantly improve on remdesivir alone; ACTT-2 had the largest benefits in that group. But in both ACTTs, there still was little to no improvement in those on mechanical ventilation.

Scientists at the University of Oxford found hopeful news for this critically ill group. Their Recovery trial revealed that dexamethasone, a corticosteroid, improved outcomes for people with severe Covid infections. Mortality decreased in the oxygen therapy groups, but the biggest benefit was seen in the mechanical ventilation group. This ongoing trial also is studying several antivirals including two repurposed HIV drugs, lopinavir and ritonavir, that have not shown benefit against Covid. Remdesivir has not, so far, been studied in the Recovery trial.

From August to November, there was an ACTT-3, to test the antiviral interferon,

Nurse Researcher Applies Lessons Learned as a Former Lobbyist

BY DIANA FINEGOLD

Dr. Sarah Szanton, health equity and social justice endowed professor at Johns Hopkins School of Nursing, did not start out as a nurse researcher. In her former life, she was a health policy advocate. During her NINR Director's lecture, "Leveraging Strengths to Achieve Health Equity: From Clinical Insight to Program of Research," she made clear how what she learned as a lobbyist could be applied to creating sustainable change in research.

Szanton's work focuses on health equity and empowering older adults to live in the place of their choice as they age, while maintaining quality of life. In her talk, she showed real-life examples of the impact and sustainability of the program she co-developed: Community Aging in Place—Advancing Better Living for Elders (CAPABLE).

In CAPABLE, the older adult is considered the expert and clinicians support the expert's goals. This strategy has been shown to increase physical function, reduce depression and allow for fewer hospitalizations and nursing home admissions.

"In CAPABLE," Szanton explained, "we address the whole person by modifying the environment and working with the person to make the best fit between the two. And that's a foundational idea in gerontology, but it often hasn't been implemented."

Several themes emerged throughout her talk: resilience and strength-based approaches rather than deficit approaches; struggle, including disability, as a source of innovation; equity throughout—including thinking structurally rather than interpersonally; using data to leverage change; and working with people as they are and wherever they are.

Szanton's role as a lobbyist provided invaluable guidance on how to take one's research and make it available to others. She explained how crucial it is to be able to see things from the next step, so a researcher can take what is learned and make it available to others.

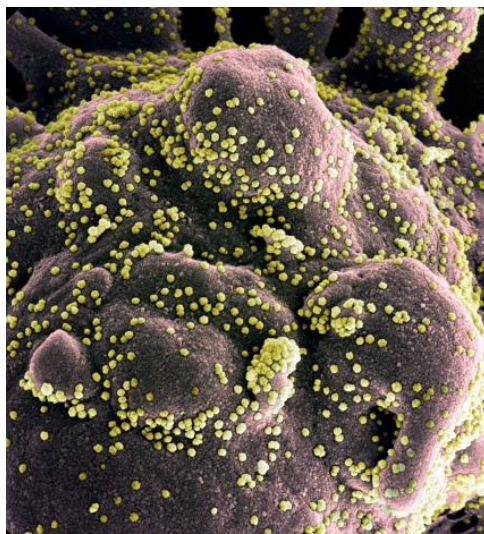
She also shared additional lessons she's learned along the way, including the importance of excelling in what matters to the people who measure your performance; building from insight; using compelling stories; and measuring cost savings or other markers of value such as employee satisfaction or nurse retention.

CAPABLE is a prime example of nursing research innovation that translates into improved health outcomes. For details, visit https://nursing.jhu.edu/faculty_research/research/projects/capable/. To watch Szanton's lecture and learn more about her work, go to <https://videocast.nih.gov/watch=41434>.

'CAPABLE'



Dr. Sarah Szanton,



This colorized scanning electron micrograph shows SARS-CoV-2 virus particles (yellow), isolated from a patient.

PHOTO: NIAID

though the results are not yet available. In December, ACTT-4 began enrolling a 1,500-patient cohort to study whether dexamethasone or baricitnib work better when paired with remdesivir among hospitalized patients on oxygen and/or noninvasive ventilation.

It's tough to compare results between ACTT, Solidarity and Recovery, said Beigel, because the design, parameters and populations are not analogous. Even mortality rates aren't comparable between the different trials.

"A drug that has a detectable effect in a population with a high risk of death may not have the same effect once you get to a lower [risk] of death," he said.

Instead, he advised considering the totality of the data and reaping the lessons from each trial, which offer important guidance for specific populations. Additionally, standard of care has improved over time which, on its own, is improving outcomes.

Researchers worldwide continue studying ways to reduce illness severity and mortality. To date, there is no fully effective treatment for Covid-19. "There's still a lot of work to be done," said Beigel. This is the value of complex trials, he continued, generating datasets and samples to permit analysis and testing to better inform how to best treat Covid-19. **B**

Share the Plants You've Grown

For many NIHers, growing plants at home has provided a welcome respite from the past year.

We'd like to hear from you about the plants you've been growing.

Send a high-resolution color photo with a brief caption explaining what the plant means to you to nihrecord@nih.gov. Scientific plant names are preferred.



Shown in a January 2020 photo are plants from the Clinical Center's department of bioethics. While staffers telework, their greenery was collected for communal tending.

Virtual

CONTINUED FROM PAGE 1

author of numerous books, most recently the 2018 bestseller, *Can You Hear Me Now?*

When we send and receive emails or texts, “we believe we are understood, and understand correctly, 90 percent of the time when, in fact, our success rate is maybe 50 percent,” he said. This disconnect is also a recurring headache with video meetings, our customary form of communication during the Covid pandemic.

“If we’re going to get through this pandemic, and this difficult period of social isolation, then we need to spend more time and take more care in understanding each other’s intentions,” said Morgan, speaking at a recent virtual Deputy Director for Management Seminar Series lecture.

What Do You Mean?

Morgan’s lifelong interest in communication began as a teenager, when his sled collided with a tree, fracturing his skull. When he awoke from the coma, he had to relearn cognitive and communication skills, including how to read body language.

Over the years, Morgan has come to realize that real-world communication isn’t easily replicated online. In person, we use social cues to sense the other person’s intent and adjust our reactions. On video meetings, many subtleties get lost and it’s harder to read body language—the nods, shrugs, knitted brows, glazed-over eyes. Lacking that feedback, all-virtual relationships tend to steadily erode, he said.

“Over time,” said Morgan, “the many little misunderstandings that come about, because of the complicated nature of the communication, gradually add up to a degradation of trust and camaraderie.”

Meanwhile, on video meetings, we’re all in 2-dimensional little boxes, so proprioception—how we perceive our spatial relation to others—is askew, and it’s fatiguing.

“By the end of the day, we’ve been in low-stress mode for a number of hours because our proprioception is going haywire trying to figure out where everybody is,” he said.

And it’s not just what we see. The audio we hear over the phone and the computer is compressed, so we’re missing the inflections and emotion gets muted. Also, without the face-to-face audio-visual



cues, we’re unsure when the other person is winding up their remarks and tend to interrupt each other more.

And, there are other elements conspiring against us, virtually.

Assuming the Worst

Our lack of feedback in the virtual world sets off a series of other communication pitfalls. Each time there’s a lag on video, during that awkward pause when we can’t quite read others’ reactions, we subconsciously assume the worst. That frustration and the ensuing misunderstandings, said Morgan, often devolve into a lack of empathy.

What’s more, there’s a virtual lack of

control. We cringe at those awkward Zoom meeting moments when kids come barreling into the room, the dog incessantly barks or your spouse’s sneezes drown out your comment. “The virtual world demands consistency,” said Morgan, “but we humans are an inconsistent species.”

And beware of another pitfall with serious consequences: virtually, the lack of emotion can impair decision-making.

“We connect hierarchies of emotion to things that tell us how important something is or isn’t,” said Morgan. “Pain is at the top; joy comes a little below that. As a result, in the virtual world, where emotions are muted, we find it harder to make good decisions.”

All of this, he said, leads to a lack of connection and diminished trust.

Making Intent Clear

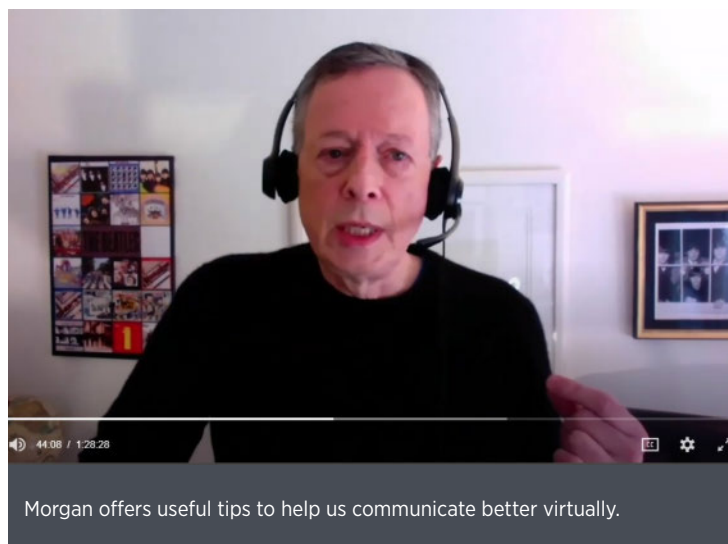
Luckily, there are actions we all can take to communicate better and forge stronger bonds online. Morgan recommends creating virtual safe spaces to emulate that



watercooler connection at the office. For some, Zoom work socials are that outlet. But, he said, many people have grown weary of them because “[socials] have an informal nature and video-conferencing demands a formal scheduling.”

Instead, he advises creating safe spaces within the meeting itself—chitchats at intervals to ask about the kids or hobbies—and preferably not at the meeting outset, when everyone is looking for their mute button while trying to connect.

Another tip: “Assign an emcee who will make sure everyone participates,” said Morgan. “People will pay attention better



“As a very crude substitute for simple body language, emojis will do the trick in the short run,” said Morgan. “So suck it up, swallow your dignity and start to use [them].”

Another email tip: make the subject heading a sentence or detailed phrase.



“We need to spend more time and take more care in understanding each other’s intentions.”

-NICK MORGAN



and participate more.” Plus it may cut down on the interrupting. The emcee, he added, should pause every 10 minutes or so—the average online attention span—to ask for input or just to mix it up.

Also, it’s a good idea to track staff morale, but you won’t find out by asking directly, said Morgan. Take the team’s temperature over time. Try a simple number scale, a red/yellow/green light check from bad to great or some other quick poll.

And, because the worst format for getting intent across is email—hear Morgan out on this one—use emojis. With a smiley face, that “nice job” message can’t be misconstrued.

“Quick question” will only elicit recipient groans. If you’re specific, and include an action item, that clarity will improve response time and efficiency.

When we return to normal, we’ll still contend with some virtual pitfalls. For now, we keep trying to adapt to our all-virtual environment.

So, try to make your intent clear and be understanding. “In the pandemic, we’ve all discovered there’s nothing wrong with being human,” said Morgan. “In fact, you might as well embrace it, because we’re all in this together.” **R**

NIMHD Announces New Textbook

NIMHD recently announced release of a new textbook, *The Science of Health Disparities Research*, edited by Drs. Irene Dankwa-Mullan, Eliseo J. Pérez-Stable, Kevin L. Gardner, Xinzhi Zhang and Adelaida M. Rosario. The publication is now available in bookstores.

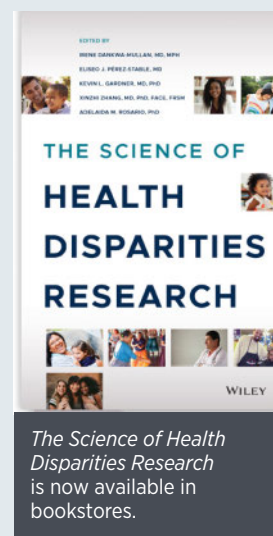
Building upon the advances in health disparities research over the past decade, this new textbook will serve as a reference to scientists developing a research program focused on health disparities research.

These strategies will inform policies and practices addressing the diseases, disorders and gaps in health outcomes that are more prevalent in minority populations and socially disadvantaged communities.

In 26 chapters, the book describes how using an interdisciplinary approach can reduce inequities in population health studies, the importance of relying on community engagement for much of the research process, and the ways that rigorous research can promote social justice.

The Science of Health Disparities Research is an essential resource for trainees and clinical researchers in health services, behavioral science, population science, public health and basic science as it intersects with clinical studies; health care policymakers and epidemiologists; and those working with minority, vulnerable or underserved populations.

For details about the book, visit <https://nimhd.nih.gov/about/publications/the-science-of-health-disparities-research.html>.





In 2014, Flint switched its water supply from Lake Huron to the Flint River (l). Even though the Flint Water Crisis is over, Hanna-Attisha said residents feel betrayed by the people who were supposed to protect them. PHOTOS: CAROL M. HIGHSMITH

Flint

CONTINUED FROM PAGE 1

“When I heard about lead, my life changed,” said Hanna-Attisha, a pediatrician and founder and director of the Michigan State University-Hurley Children’s Hospital Pediatric Public Health Initiative, during a recent NIMH Director’s Innovation Speaker Series. “I became really consumed with what was happening with my Flint kids and how to best protect them.”

Thanks to the auto industry, Flint was once home to a thriving middle class. Like so many other post-industrial towns across America, the city suffered from decades of disinvestment and population loss. Now, 69 percent of Flint’s children under age five live in poverty.

During a budget crisis in 2014, the city switched its water supply from Lake Huron to the Flint River. After the change, residents began to raise concerns about the water’s color, odor and taste. In addition, the switch also led to an outbreak of Legionnaires’ disease that killed 12 people. The disease causes a serious form of pneumonia.

At first, Hanna-Attisha assured her patients the water was safe because “there

are people who wake up every day—who our tax dollars support—to make sure that when I turn on my tap in Flint or Bethesda or wherever I am, that my water is safe.” Her opinion soon changed.

Once her friend tipped her off about lead in the water, she had to act because

“I knew that if I was going to make a difference, I would need science, data and facts in my pocket,” Hanna-Attisha said. “I quickly conducted the research to see if there was more lead in the bodies of our children.”

She reviewed blood for children younger than age five before and after Flint’s water

source change and found that area kids’ blood lead levels were higher after the change. Disadvantaged areas had the greatest increases in blood lead levels. She knew she couldn’t afford to wait to present her research in an academic journal because the publishing process was too long.

“I did something most doctors and scientists don’t usually do,” said Hanna-Attisha. “I literally walked out of my clinic with my white coat on and stood up in one of our hospital conference rooms where we usually have resident lectures. I shared the

research that our kids are in harm’s way and I demanded action.”

After her press conference, state officials accused her of “slicing and dicing” data and “causing near hysteria.” They claimed her data set differed from theirs.

“I felt absolutely tiny and defeated. I began to second guess myself,” she recalled.



Dr. Mona Hanna-Attisha (top l) speaks with NIMH director Dr. Josh Gordon (top r), Dr. Alexander Denker and an ASL interpreter.

there is no safe amount of lead for kids. Lead exposure can cause serious harm to children’s health, including damage to the brain and nervous system, delayed growth and development, and learning and behavior problems. In turn, these result in lower IQ, decreased ability to pay attention and underperformance in school.

“I think, especially so many women, we often talk about imposter syndrome. I felt like I shouldn’t have done this. Fortunately, I quickly realized this doesn’t have anything to do with me.”

This was about research, data and evidence. Each number wasn’t just a number—it was a child. “It was as if those kids jumped out of my spreadsheets, lifted me up and gave me the courage to keep going,” she said.

Eventually, the state concluded that their research was consistent with Hanna-Attisha’s findings. A federal emergency was declared to support the response to the water crisis and recovery. The state of Michigan and private donations also provided support.

“I don’t want to be vindicated,” she said. “I just want the kids to be protected. Our kids never should have had to go through this. I’m glad that we were able to expose all this, but it never should’ve happened in the first place.”

Flint residents feel betrayed by the people who were supposed to protect them, she added. They’re still angry. Many parents experience guilt because they gave contaminated water to their children.

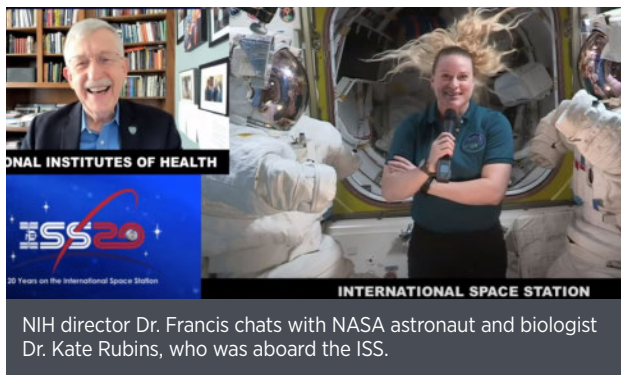
At the height of the crisis, she was hardly ever home for her own two young daughters. They recognized that their mother was with their 6,000 siblings.

“I’ve been able to persevere with villages of support both at home and at work,” Hanna-Attisha said. At work, she surrounds herself with smart coworkers. At home, she has people who can help out and a list of babysitters. “It’s definitely not easy.”

For many working mothers, the Covid-19 pandemic “has thrown the idea of balance out the window.” It’s difficult for them to work and advance their careers while also caring for children.

Today, Hanna-Attisha is focused on developing programs that improve the health and development of children, including early education, health care, child care programs and parental education programs. For example, the nutrition prescription program she helped develop provides a \$15 voucher for fruits and vegetables at a farmer’s market to every child who visits a health clinic.

“I don’t want to be known for uncovering the water crisis,” Hanna-Attisha said. “I want to be known for what we did next, which is our recovery.” **R**



LOW-TECH REMEDIES TO THE RESCUE

Astronaut Updates Collins on Scientific Progress Aboard ISS

BY ERIC BOCK

Velcro and tape are advancing molecular biology in microgravity, the unique environment where the effects of Earth’s gravity are minimal, said NASA astronaut and biologist Dr. Kate Rubins while aboard the International Space Station.

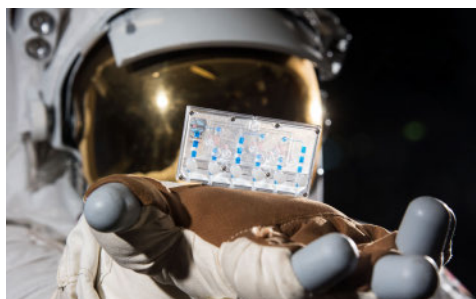
“One of the hardest parts about doing laboratory science here is that you can have a bench, but nothing will stay on the bench,” said Rubins, during a recent chat with NIH director Dr. Francis Collins. “It moves around, and it walks away and it floats off the second you stop looking at it.”

These low-tech solutions allow astronauts to understand health, disease and aging in space and the implications on Earth and to sequence the DNA of microbes that live on the space station.

“We’re all fascinated by the way in which science is being conducted there on the International Space Station,” said Collins.

Since 2016, NCATS has partnered with NASA to launch the Tissue Chips in Space initiative. Tissue chips are tiny 3-D models that contain living human cells, such as heart or bone, grown on an artificial scaffold. These chips mimic essential functions of the human body.

“These tissue chips are super exciting for understanding the effects of space flight on the human body. But it’s not just all about NASA,” Rubins explained. “One of the things that we’re looking at



Since 2016, NCATS has partnered with NASA to launch the Tissue Chips in Space initiative.

IMAGE: NCATS

with these is how we can replicate some disease processes on Earth.”

Collins said biomedical researchers are always looking for disease models that more accurately represent human physiology and pathology.

One such study using a cartilage-bone-synovium joint tissue chip focuses on the effects of microgravity on musculoskeletal diseases, such as osteoarthritis and bone loss.

In microgravity, astronauts lose bone density. Once they return to earth, astronauts regain their bone density. However, the trabecular structures—what gives bones their strength—do not come back even in healthy, younger space travelers. To counteract these effects, Rubins said, astronauts lift weights.

The bone loss astronauts undergo in space is similar to bone loss that older adults experience on Earth. Because these physiological changes happen more quickly in microgravity than they do on Earth—reducing the timeline from years to months or even weeks—using tissue chips in space to study bone loss could speed the discovery of therapeutics that prevent cartilage and bone loss resulting from the normal aging process.

During an earlier stay aboard the ISS, Rubins demonstrated for the first time that it’s possible to sequence DNA in space. Her lab features a small sequencer the size of a cell phone because “larger sequencing machines are just not super suitable for the space environment.”

One of the reasons for conducting the experiment was to identify microorganisms living on the ISS in real time. Previously, astronauts swabbed surfaces aboard the ISS, put the samples on a culture and sent them back to Earth for identification. The process depended on when a space vehicle returned to Earth.

Right now, she is using a method called multiplex sequencing to identify what lives in the richest microbial locations (including the astronauts themselves) on the ISS. There is no dirt on the ISS and supplies are packaged in cleanrooms before they are sent up to the station to reduce microbial counts.

Once she has data, Rubins hopes to determine what microbes grow best in microgravity and radiation and learn more about astronauts’ microbiomes. In the future, the technology might be one tool of many to help identify unknown DNA-based life forms on other planets.

“This is the best time to be a scientist in the history of the planet because so many things are possible even on planet Earth and even in the space station,” said Collins. Rubins agreed, “It’s truly amazing to get up and discover new things.”

This was their second “space chat.” Rubins has also visited NIH to celebrate National DNA Day to talk about science in space. **R**

NIH Team Develops Language Test for People with Down Syndrome

An NIH research team developed a test to evaluate the expressive language skills of people with Down syndrome, a condition resulting from an extra copy or piece of chromosome 21. Language delays are common in people with Down syndrome. The study authors believe their test could more effectively evaluate prospective language interventions. The study, funded by NICHD and NCATS, appears in the *Journal of Neurodevelopmental Disorders*.



NICHD explores better ways to evaluate expressive language in people with Down syndrome.

IMAGE: DENKUAIEV/ISTOCK/GETTY

The 107 study participants ranged from 6 to 23 years old, and all had an IQ of 70 or less. Researchers engaged the participants in conversation, which was recorded, transcribed and scored on the basis of talkativeness, vocabulary, sentence structure and other aspects of spoken language. When the participants repeated the same test 4 weeks later, test scores were consistent, an indication of the test's reliability.

Participants whose language was limited to basic phrases and those who had a developmental level below 4 years of age had difficulty completing the test. Additional studies are needed to develop

other measures for those with more limited spoken language skills.

SARS-CoV-2 May Infect Mouth Cells

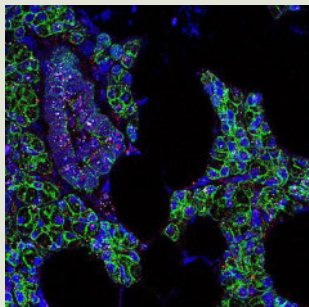
NIH researchers recently found that SARS-CoV-2, the virus that causes Covid-19, can infect cells in the mouth. The results appeared online in *Nature Medicine*.

“By revealing a potentially underappreciated role for the oral cavity in SARS-CoV-2 infection, our study could open up new investigative avenues leading to a better understanding of the course of infection and disease,” said senior study author Dr. Blake Warner, chief of the salivary disorders unit at NIDCR. “Such information could also inform interventions to combat the virus and alleviate oral symptoms of Covid-19.”

Researchers were curious whether the virus-laden saliva of Covid patients might come from infected tissues in the mouth, rather than from nasal drainage or material coughed up from the lungs.

The researchers first studied oral tissues from healthy people to determine whether mouth cells were susceptible to SARS-CoV-2 infection. RNA molecules that provide the instructions for cells to make certain proteins, which the virus uses to get into cells, were found in certain mouth cells, including glands that produce saliva and the tissues lining the oral cavity.

The team then looked for evidence of infection in oral tissue samples from Covid-19 patients who had died. SARS-CoV-2 RNA was present in more than half of the salivary glands. Further experiments showed that, in people with mild or asymptomatic Covid-19, cells shed from the mouth into saliva contained SARS-CoV-2, as well as RNA for the viral entry proteins.



RNA for SARS-CoV-2 was found in salivary gland cells.

IMAGE: PAOLA PEREZ, NIDCR

When researchers exposed saliva from people with asymptomatic Covid-19 to healthy cells grown in a dish, saliva from some volunteers infected the healthy cells. Among people with mild Covid-19, those with virus in their saliva were more likely to report loss of taste and smell.

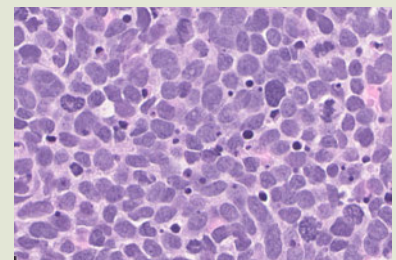
Together, these findings suggest that the mouth, via infected oral cells, may play a bigger role in SARS-CoV-2 infection than previously thought. Saliva infected by these cells might infect the lungs when breathed in and the gut when swallowed.—adapted from *NIH Research Matters*

Researchers Make Advances in Treating Small Cell Lung Cancer

NIH researchers have identified and tested a drug combination that exploits a weakness in small cell lung cancer (SCLC). The scientists targeted a vulnerability in how the cancer cells reproduce, increasing already high levels of replication stress—a hallmark of out-of-control cell growth in many cancers that can damage DNA and force cancer cells to constantly work to repair themselves. In a small clinical trial, the drug duo shrank the tumors of SCLC patients. The team reported its findings in *Cancer Cell*.

While many patients with SCLC initially respond to chemotherapy, they usually live a matter of weeks after their first treatment stops working and this aggressive cancer returns. Scientists at NCI and NCATS teamed up to find another option.

The NCI group explored the potential of nearly 3,000 agents from an oncology-focused library of investigational and approved drugs against SCLC cells. NCATS's robotics-enabled, high-throughput screening technologies allow scientists to rapidly test thousands of different drugs and drug combinations. Scientists can examine the most promising drugs and drug combinations, determine effective dosing and learn more about the possible drug interactions.



Small cell lung carcinoma cells

IMAGE: PARTH DESAI, NCI

The research team found multiple combinations involving commonly used chemotherapy drugs that cause DNA damage and drugs designed to block DNA repair. One of the most effective combinations was FDA-approved chemotherapy drug topotecan and an investigational drug M6620, or berzosertib, which blocks an enzyme, called ATR, that plays a role in DNA repair.

“Blocking the ATR enzyme means cancer cells can't respond to DNA damaging agents properly,” said NCATS translational scientist Dr. Michele Ceribelli, co-author of the study. “This makes chemotherapy even more effective.”

The NCI researchers tested the berzosertib-topotecan drug combination in a clinical trial involving SCLC patients who either had relapsed after initial treatment or for whom their therapy had stopped working. They found the drug combination helped more than one-third of participants (9 of 25) improve in some way. In some cases, the improvement lasted for 6 months.

The findings suggest that researchers could develop a more personalized approach in treating SCLC as well as other types of small cell neuroendocrine cancers. As a next step, NCI is sponsoring a larger clinical trial to compare the effects of berzosertib and topotecan in combination against topotecan alone in SCLC patients.

CSR's Lockett Retires After 30 Years at NIH

BY JEANNINE MJOSETH

Don Lockett is retiring as communications director at the Center for Scientific Review with 30 years of service, though he initially refused the job that launched his NIH career.

Armed with a great liberal arts education from Earlham College in Richmond, Ind., Lockett had anticipated more than \$6.50-an-hour temping at NIH. But he acquiesced, having spent the previous 10 years painting houses and writing the great (unpublished) gay American novel.

He landed in the Office of AIDS Research as the numbers of people dying from AIDS soared. There, he served as secretary to Dr. Jack Whitescarver, who managed OAR for Dr. Anthony Fauci.

"Phones rang, acronyms flew and every document that went to Dr. Fauci landed on my desk," Lockett said. "I took up the challenge with a blue/red pencil and sent edits back to the staff scientists. It wasn't long before they hired me as a writer/editor."

The work was meaningful and he loved the staff camaraderie. He especially enjoyed responding to letters. He carefully replied to those who thought they'd found the cure for AIDS in their garage laboratories, and he often went above and beyond.

"I managed to get a gravestone for an orphaned AIDS child who was beloved by Clinical Center staff," he recalled. "I often told patients, lovers and family members how the NIH cavalry was on the move. I silently wept over the many courageous souls fighting AIDS—awed at what NIH was doing, but knowing we might be too late for them."

When CSR needed a communications director in



Don Lockett retires as CSR communications director with 30 years of service.

2000, he jumped at the new challenge and stayed on to serve four directors. He has helped many scientists navigate their grant application reviews and promoted many interesting projects to enhance peer review.

He asked countless people across CSR and NIH to help advance these initiatives. "I retire with incredible gratitude for all those who said yes over the years," Lockett said.

He has never tired of telling NIH's story: how finding and funding prom-

ising research has saved and improved millions of lives, and how investing in peer-reviewed, basic research pays huge dividends down the road. Twice, he was thrilled to join then CSR director Dr. Richard Nakamura to bring this message to Capitol Hill.

Storytelling is in Lockett's blood. One of his favorites is about the NIH review



Recently, Lockett helped CSR develop the NIH Scientist Launch Game app—www.csr.nih.gov/rocket.

committee that awarded a \$10 "grant" to two kids requesting funds to build a rocket ship in 1957. The payoffs were impressive, and Lockett thought the story could get children excited about NIH and science. So he wrote and oversaw the development of a children's book and cartoon. More than 32,000 copies of the book were distributed at the annual NIH Take Your Child to Work

...
"I've had a front row seat to the development of science that has saved millions, and I've made such wonderful friends."

-DON LOCKETT

Day celebrations and the USA Science and Engineering Festivals.

More recently, CSR joined with NIAID, NCI and NHLBI to develop the NIH Scientist Launch Game app—www.csr.nih.gov/rocket.

Lockett's also done yeoman's work leading the development of videos with more than 200,000 YouTube views. He launched a webinar series for applicants that won an NIH Director's Award in 2015. His last act before leaving was to help NIH celebrate CSR's 75th anniversary with a soon-to-be-released video—*Catalyst of Hope and Health: 75+ Years of NIH Peer Review*.

"I've had a front row seat to the development of science that has saved millions, and I've made such wonderful friends," Lockett said. "It's been such a privilege, but it's time to pass the torch to the next generation. I'm looking forward to writing books, visiting friends and exploring other ways to do good." **R**

60 YEARS LATER

Reconnecting with First NIH'er to Join the Peace Corps

BY JOHN SCHELP AND PETER KILMARX

Back in 1961, the *NIH Record* ran a story about a young researcher who was leaving Bethesda's leafy campus to join the Peace Corps.

Since then, hundreds of Peace Corps volunteers have come to work at NIH. An affinity group of returned Peace Corps volunteers (RPCVs) at NIH was formed in 2015.

On the occasion of the 60th anniversary of the Peace Corps, they saw the *Record* article and wondered, "Whatever happened to that young researcher?" They tracked her down and found Dr. Judith McKay Sides happily ensconced in the Appalachian Mountains of western North Carolina, where she readily agreed to join the group's monthly Zoom call and share some stories.

"I'm 82 years old now and I like to boil things down," Sides began. "Naturally, researching at NIH and volunteering in Peace Corps were major highlights 60 years ago. It seems like yesterday."

Her first paid job was at NIH's National Institute of Arthritis and Metabolic Diseases (now NIAMS).

"I was a GS-5 at \$5,000 per year," she recalled. "I rented a tiny spare bedroom at somebody's house in Bethesda, slept on a stretcher, ate hard-boiled eggs and drank vegetable soup from cans."

Sides recalled working as a laboratory assistant



Dr. Frederick Stohlman and Dr. Judith McKay Sides study the World Atlas that the NIAMD Laboratory gifted her so they could look up the location of Nigeria, 1961.

to Dr. Frederick Stohlman, "a large, brilliant man," the editor of *Blood* magazine, studying erythropoiesis.

"Our source of erythropoietin was Randy, a 10-year-old boy suffering aplastic anemia with very high levels of the hormone in his urine," Sides recounted. "My job was to condense gallons of Randy's valuable urine, extract his erythropoietin,

and prepare different concentrations to inject into rats. At my first evaluation with Dr. Stohlman, he requested that I stop carrying two big flasks of Randy's priceless urine at a time and spend less work time reading articles about our experiments. I should do that at home."

In January 1961, Washington was abuzz about Kennedy's inauguration. A colleague at NIH had several tickets to be a hat-check girl at 1 of the 5 inaugural balls. Sides remembered the snowy night at the D.C. National Armory.

"We were paid \$25 each," she said. "The armory was packed with 14,000 people. Jackie Kennedy was recovering postoperatively from a Cesarean section, so the presidential couple did not dance. That evening was a blast. I bought snow boots with my \$25."

Sides was in only the third group of Peace Corps volunteers to fly out to their host country. She was assigned to Nigeria, shortly after its independence, where she taught piano and anatomy—using a standing cow skeleton they



Sides speaks during an Apr. 6 Zoom call with returning Peace Corps volunteers at NIH.



Nigeria 2 Peace Corps volunteer group en route to the airport in November 1961. Sides is in the second row from bottom (sixth from l).

assembled—at the newly opened University of Nigeria campus in Nsukka.

After her Corps service, she earned a medical degree at Tufts Medical School, where Stohlman was then on the faculty, and later went into practice in Marblehead, Mass.

As Sides reminisced, the Zoom audience was enthralled.

"Here is my essence," she summarized, "Be friendly, useful, helpful, apolitical, make do and have fun."

It was a wonderful way to mark the Peace Corps' 60th anniversary, linking together the first NIH RPCV with the current generation, celebrating the continuous themes of inquiry and service.

See Sides' article in the *Record* at <https://nihrecord.nih.gov/sites/recordNIH/files/pdf/1961/NIH-Record-1961-08-29.pdf>. Returned Peace Corps volunteers at NIH are encouraged to join the affinity group at https://list.nih.gov/cgi-bin/wa.exe?AO=rpcvs_at_nih.