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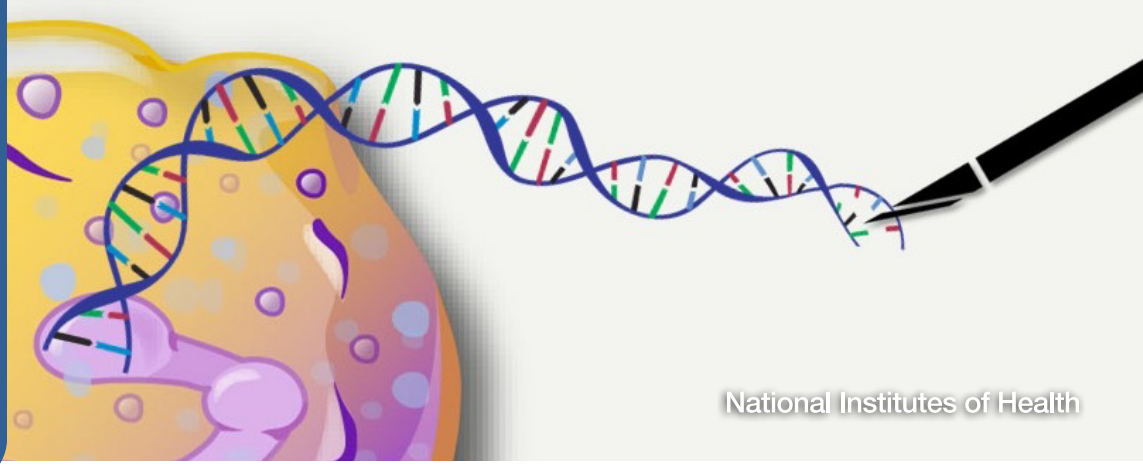


HARNESS THE POWER

Chief Internet Evangelist Cerf Discusses AI at NIH

BY CARLA GARNETT

A world-renowned professor of any scientific field tends to draw a large NIH congregation composed of both seasoned believers as well as the merely intellectually curious. That's what happened Mar. 19 as Google's Chief Internet Evangelist Dr. Vinton Cerf took to the Masur Auditorium pulpit for the 2024 J. Edward Rall Cultural Lecture.

Titled the "Promises and Perils of AI in Biomedical Research and Health Care Delivery," Cerf's 15-minute "sermon"—his word—attracted a huge mix of IT experts, acolytes and neophytes and preceded a wide-ranging fireside chat with NIH Director Dr. Monica Bertagnolli.

Google's Dr. Vinton Cerf gives the 2024 Rall Cultural Lecture at NIH.

PHOTO: LESLIE KOSSOFF

"At NIH, I very much hope for all of us to work together to deliver evidence-based health care to all people and I'm very excited about how new techniques in machine learning and artificial intelligence can help us advance toward that goal," Bertagnolli said, in opening remarks.

Introducing the guest speaker, she recalled her personal experience as a surgical oncologist and clinical investigator working to integrate standardized biomarkers into research trials—"a complicated enterprise trying to mix basic science endpoints including complex genomics and clinical data."

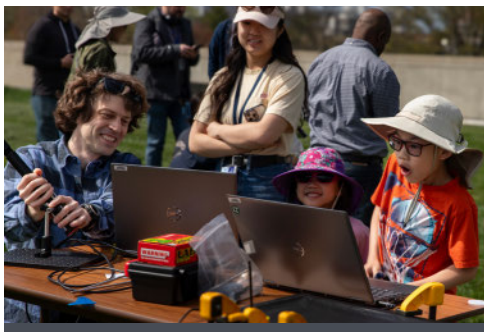
At the lectern, Cerf described himself as "a networking guy, not an expert in AI." However, he noted that Google, the company he's worked for since 2005, has invested a lot of time and resources in the artificial intelligence field.

Emergence of AI

"Major progress has been made—especially in machine learning," he said.

Cerf briefly retraced development of AI. The field began with problem-solving

SEE **CERF**, PAGE 6



Solar eclipse draws wow factor at NIH. See p. 11.

ALSO THIS ISSUE

WOMEN AFFECTED MORE

Pelvic Floor PSA

BY AMBER SNYDER

Between a quarter and half of all women may experience pelvic floor issues, yet many accept it as a fact of life or feel embarrassed about seeking help. How do we improve outcomes?

Pelvic Floor Disorders

Pelvic floor disorders (PFD) are a broad range of conditions affecting the pelvic organs such as the bladder, bowels and reproductive tract. These conditions include urinary leakage or frequency, urinary or fecal incontinence, and pelvic organ prolapse. PFDs

PFDs can affect the reproductive tract and other pelvic organs.

SEE **PELVIC**, PAGE 8

Platt Explores Softer Side of Bioengineering

BY DANA TALESNIK

Dr. Manu Platt has a reputation for exuding enthusiasm when talking about his work. The biomedical engineer recently delivered an animated presentation that spanned his work on tissue remodeling, which underpins his research toward finding new therapies for sickle cell disease (SCD).

Dr. Manu Platt

Platt arrived at NIH a year ago to launch the BETA (Biomedical Engineering and Technology Acceleration) Center, an NIH-wide data resource and community to accelerate

SEE **PLATT**, PAGE 4

June 5

Barmes Global Health Lecture Returns

The National Institute of Dental and Craniofacial Research and the Fogarty International Center will present the 2024 David E. Barmes Global Health Lecture, "Global HIV/AIDS Response: Then, Now, Future," by Ambassador John Nkengasong, U.S. global AIDS coordinator and special representative for global health diplomacy. The lecture will take place in on Wednesday, June 5 at 1 p.m. ET in Kirschstein Auditorium, Natcher Conference Center, and be livestreamed via NIH videocast.

Ambassador John Nkengasong

Closed captioning will be available to all participants. Individuals who need reasonable accommodation to participate in this event should email FICInfo@mail.nih.gov or phone (301) 827-7631. Find event details at https://go.nih.gov/Barmes2024.

Networking opportunities abound at an OITE career event in 2017.

PHOTO: DANIEL SOÑÉ

Annual NIH Career Symposium Scheduled

NIH's Office of Intramural Training and Education (OITE) invites all NIH graduate students and postdoctoral trainees, both basic scientists and clinicians, to participate in the annual NIH Career Symposium to be held virtually May 14-17.

The symposium provides career exploration and networking opportunities for graduate students, postdocs and fellows in the Intramural Research Program. Graduate students and postdocs from outside NIH are also welcome to attend. A range of panels, interviews and discussions with speakers from across the biomedical workforce will be presented.

Registrants will have the opportunity to network with peers and professionals in different career paths. OITE staff will present strategies for navigating the job search and its ups and downs. Each day will focus on a different theme and registrants are welcome to attend everything, or just watch the sessions that appeal to them.

For more information and registration, visit https://www.training.nih.gov/me/cs/.

At this year's Rx and Illicit Drug Summit, NIH Director Dr. Monica Bertagnolli (l) and NIDA Director Dr. Nora Volkow give presentations.

PHOTOS: DALE MORTON FOR OPERATION UNITE

Bertagnolli, Volkow Present at Rx Summit

NIH Director Dr. Monica Bertagnolli and National Institute on Drug Abuse Director Dr. Nora Volkow traveled to Atlanta for the annual Rx and Illicit Drug Summit, which was held Apr. 1-4 at the Georgia World Congress Center. The summit is the largest national collaboration of professionals from local, state and federal agencies, business, academia, treatment providers and allied communities affected by prescription drug misuse and illicit drug use. Bertagnolli presented an "NIH Update: Toward Evidence-Based Care for Addiction and Beyond." She discussed her guiding principles and priorities as NIH director and gave some background on NIH's Helping to End Addiction Long-term® (HEAL) Initiative. Volkow's presentation title was "Translating Science into Action to Address the Overdose Crisis." Both leaders also served on plenary panels.

NIH Leave Bank Celebrates 10th Anniversary

The Office of Human Resources announces the 10th anniversary celebration of the NIH Leave Bank Program. After a highly successful pilot program was implemented for a handful of institutes and centers from 2010 to 2013, the Leave Bank was rolled out NIH-wide on Jan. 12, 2014 and became available to all NIH federal employees.

In its first decade serving all of NIH, the program has provided paid leave to more than 1,840 employees experiencing personal or family medical emergencies. Visit https://go.nih.gov/Jnjihb3 to read several success stories.

Throughout this timeframe, enrollment in the Leave Bank has grown from just over 4,200 members in 2014 to an incredible 12,228 in 2024.

"The Leave Bank allows us all to act as stewards in our own community and aligns effortlessly with the NIH mission," reported program coordinators in the NIH Office of Human Resources. "We would like to thank every member and donor for your support of this important benefit during our first 10 years and look forward to continuing to support the NIH community."

For further information on the NIH Leave Bank, visit the website at https://go.nih.gov/az5alK8 or email LeaveBank@od.nih.gov.

Visit Postbac Poster Day, May 1-2

NIH Postbaccalaureate Poster Day will take place on May 1-2 in Natcher Conference Center, Bldg. 45. Intramural postbacs will share the research they have been conducting. Posters will be judged by teams of graduate students, postdocs and staff scientists/clinicians. Authors of the top 20 percent will be acknowledged with a letter. Investigators, staff scientists and scientific administrators make a particularly important contribution by visiting posters and engaging authors in discussion. For details, visit https://www.training.nih.gov/me/ppd/.

Bertagnolli Leads NIH Visit to West Virginia University

NIH Director Dr. Monica Bertagnolli joined U.S. Senator Shelley Moore Capito (R-W.Va.) on a visit to West Virginia University (WVU) on Mar. 27.

U.S. Sen. Shelley Moore Capito (R-W.Va.) with NIH Director Dr. Monica Bertagnolli (c) and Dr. Ming Lei (r), vice dean of research at the WVU School of Medicine, in Morgantown, W.Va. during a series of visits at West Virginia University (WVU) Health Sciences Campus.

At WVU's Health Sciences Campus in Morgantown, Bertagnolli shared some of her priorities for improving health in the nation by getting NIH's research to more communities. She also had discussions with WVU health sciences researchers, patient care providers and university leaders, and toured several areas, including the WVU Cancer Institute's LUCAS mobile screening unit.

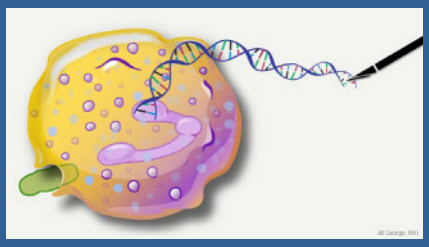
"It was truly inspiring to witness firsthand the NIH-supported research being conducted at WVU," said Bertagnolli. "The university's impressive research portfolio spans a variety of areas, including studying community-engaged amputation prevention in rural patients with diabetes, testing a precision medicine approach for treating breast cancer and researching a vaccine for Lyme disease... West Virginia faces a number of health issues that NIH-funded research is working to address to benefit the health of West Virginians and all Americans."

Other NIH'ers on the visit included Dr. Jon Lorsch, director of the National Institute of General Medical Sciences; Dr. Tara Schwetz, NIH deputy director for program coordination, planning and strategic initiatives; and Kate Klimczak, NIH associate director for legislative policy and analysis.

Dr. Tara Schwetz (l), NIH deputy director for program coordination, planning and strategic initiatives; and Dr. Jon Lorsch (fourth from l), director of the National Institute of General Medical Sciences; join Capito (c) and Bertagnolli (fourth from r) in a meeting with West Virginia leaders, including U.S. Sen. Joe Manchin (D-W.Va., third from r); Dr. Clay Marsh (second from r), chancellor and executive dean for WVU Health Sciences; and Lei (r), during a visit at WVU Health Sciences Campus on Mar. 27.

The NIH group toured several areas of the Morgantown campus, including the WVU Cancer Institute's mobile lung cancer screening unit, LUCAS.

PHOTOS: WVU



ON THE COVER: *Illustration of an infection-fighting cell called a neutrophil. In this artist's rendering, the cell's DNA is being "edited" to help restore its ability to fight bacterial invaders.*

IMAGE: JILL GEORGE (USING IMAGES FROM NHGRI AND NIAID)

The NIH Record

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NIH National Institutes of Health
Turning Discovery Into Health

Platt lectures in Porter Neuroscience Center.

PHOTO: RAY MACDOUGALL/NIBIB

Platt

CONTINUED FROM PAGE 1

tech-driven, interdisciplinary research.

"But the other part of my job, which was the enticing part of coming to NIH from Georgia Tech," he said, "was I still get to run my research lab," called MATRICES (Mechanics and Tissue Remodeling Integrating Computational and Experimental Systems).

Platt began the talk by professing his fascination with his field, which encompasses much more than the imaging techniques people usually associate with the specialty.

"There's the softer side of biomedical engineering," he said at the lecture, "Strokes with Sickle Cell Disease: Dynamic Interplay Between Biomechanical and Biochemical Stimuli," held in the Porter Neuroscience Center. "It's using math and physics to solve health-related problems."

Platt's lab studies the degradation of proteins, which can lead to clogged arteries and other forms of degeneration and disease. There are many kinds of enzymes that degrade other proteins, he explained. His lab focuses on cathepsins—the most potent collagenases—which break down collagen in damaged tissue. Inhibiting cathepsins could potentially stimulate healthy tissue growth.

Pharmaceutical companies have tried developing cathepsin inhibitors; 16 of them were tested in human clinical trials.

"Sadly, zero made it through FDA approval and into our medicine cabinets," Platt said. "Many of these drugs failed not because they weren't efficacious...but due to [serious] side effects."

The failure to date of approved cathepsin inhibitors led Platt's lab to try to quantify the amount of active cathepsins, which is critical for proper dosing.

They turned to zymography—an inexpensive activity method—to look at different cathepsins implicated in tissue-destructive diseases. His lab developed a computational kinetic model enabling them to detect the amount of active protease in multiple types of cathepsins at once. This was a strategy that traditional biochemists had not pursued previously.

"The biochemists [developing the inhibitors] were looking at one enzyme and one substrate and we know the cells release more than one at a time, and we were concerned about side effects," he said.

From their experiments, Platt's team identified a process called cathepsin cannibalism, in which one cathepsin degrades another instead of just degrading its target. The finding changed their algorithm. "Now we had an actual mechanism," he said, which may improve drug research.

"I love mathematical modeling," Platt said. "When it became clear you could save on experiments, [by first] figuring out what things were not at all possible, I said, 'Sign me up!'"

Additional experiments are underway to understand and correct what's behind the inhibitor's off-target effects.

Platt is also applying this research to help find new solutions to SCD, an excruciatingly painful, inherited blood disorder caused by a mutation in hemoglobin—the iron-rich protein in red blood cells that delivers oxygen throughout the body.

In SCD, red blood cells are extra sticky. They accumulate, become sickled in the capillaries, get stuck and block blood flow.

SCD puts patients at high risk for stroke and is the biggest cause of childhood stroke. Children at greatest stroke risk need a monthly blood transfusion. Platt's lab is looking at the biomechanics of blood flow patterns to help find alternative treatments.

The cerebral vasculature is bendy and twisty, Platt explained. At sharp turns, blood flow changes and puts blood vessels at risk for remodeling. Cathepsins are turned down or off under unidirectional blood flow, he said.

"It's a great protective mechanism...so blood flow stays open as long as possible before plaque overgrows," he said. But under sites of disturbed flow, cathepsins turn up to remodel the artery that leads to stroke. Could inhibitors block the path to prevent cathepsins from degrading collagen and elastin in the artery wall?

Using MRA (magnetic resonance angiography) to reconstruct the cerebral arteries of children, Platt saw that inflammation led to increased proteases that would remodel the artery wall. They also found a signaling pathway that turned on a specific cathepsin downstream of sickle cell. If they had a JNK (pathway) inhibitor, they could reduce that cathepsin signal. Now, they have a drug target.

About 11% of children with SCD have a major stroke by age 16. Children with SCD between ages 2 and 6 are at greatest risk.

"That's the greatest risk for infarctive [silent] stroke," he said. "Then the risk goes away but by the time patients begin to hit

Platt's lab studies how tissues transition from healthy to a diseased state. Of particular interest are enzymes known as proteases, which degrade extracellular matrices and other proteins.

IMAGE: MATRICES/NIBIB

their early 20s, they are now at their greatest risk for hemorrhagic stroke. When we start to see their arteries become expansive and blown out, we're seeing this aneurism—or remodeling—that could be putting those individuals at risk for hemorrhagic stroke."

To try to understand why children are at greatest risk of arterial remodeling and stroke, Platt's team uses a cone-and-plate apparatus in their lab to recreate blood flow profiles. They can then culture the cells over time and do biochemical analysis.

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"The enticing part of coming to NIH...was I still get to run my research lab."

-DR. MANU PLATT

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Further experiments with sickled mice injected with JNK inhibitor daily from 1-3 months old protected the elastin in the artery wall but did not produce the intended effect of preserving the mechanical properties of the artery wall.

"This is why you test hypotheses," said Platt. They then went out to 5 months and found a JNK inhibitor protected collagen in the artery wall, protecting the vasculature from remodeling and loss of its mechanical integrity.

A few months ago, the FDA approved the first gene therapy to treat SCD.

"This is fantastic, but this would still require the patient to undergo a hematopoietic stem cell transplant (HSCT)," Platt said. "So we have been doing studies looking at, even after HSCT, [whether] the mice's cerebral vasculatures are protected from further elastin and collagen loss, or does some of that earlier damage, once initiated, continue?"

Combining elements of biochemistry and bioengineering, Platt's experiments continue toward understanding and reversing tissue degradation that underlies stroke risk in SCD and the progression of other diseases. His lab's goal is to develop effective, accessible treatments that make it into the medicine cabinets of people who need them around the globe. R

GLOBAL HEALTH

Neuzil Named Director of Fogarty International Center

Dr. Kathleen Neuzil has been appointed as the 13th director of the Fogarty International Center (FIC) and NIH associate director for international research. She will be the first woman to hold the center's permanent directorship since FIC was founded in 1968.

Dr. Kathleen Neuzil

Currently serving as the Myron M. Levine endowed professor in vaccinology; director of the Center for Vaccine Development and Global Health; and chief of the Division of Geographic Medicine at the University of Maryland School of Medicine, Baltimore, Neuzil is expected to join NIH in early May.

"Dr. Neuzil has decades of experience in global health, specifically in vaccinology," said NIH Director Dr. Monica Bertagnolli, announcing the appointment. "Her impressive research portfolio includes clinical and epidemiological studies into dozens of infectious diseases. Combined with her many years as a vaccine policy advisor to the Centers for Disease Control and Prevention (CDC) and the World Health Organization (WHO), and her experience establishing new partnerships and directing diverse organization teams, she is very well suited to lead FIC."

Neuzil will lead Fogarty in its mission of supporting and facilitating global health research conducted by U.S.-based and international investigators, building partnerships between health research institutions across the globe and training the next generation of scientists to address global health needs. She will oversee FIC's annual budget of approximately $95 million, the majority of which is distributed through the center's grant programs.

Neuzil's robust research portfolio features more than 330 scientific publications on vaccines and infectious disease research. She has received NIH and other governmental and philanthropic funding throughout her career and has led collaborative research programs on a variety of diseases, including influenza, typhoid and Covid-19. She has established partnerships to address cross-cutting issues such as maternal immunization, optimizing vaccine use and ensuring sustainable vaccine uptake in low-resource settings. She has a strong commitment to mentoring the next generation of scientists and leaders in the field.

Neuzil received her undergraduate degree in zoology from the University of Maryland, College Park. She earned her M.D. from Johns Hopkins University School of Medicine and completed her internship and residency at Vanderbilt University School of Medicine.

While at Vanderbilt, she also completed a fellowship in infectious diseases and earned her master's in public health. She is a member of the National Academy of Medicine and the WHO Strategic Advisory Group of Experts on Immunization. She also previously served on CDC's advisory committee on immunization practices.

Bike to Work Day Set for May 17

The NIH Bicycle Commuter Club and the Division of Amenities and Transportation Services will host Bike to Work Day on Friday, May 17 in front of Bldg. 1 from 7 to 8:30 a.m. ET.

Join friends and colleagues to celebrate bicycling as an environmentally friendly, fun and healthy alternative to driving.

To register for the pit stop in front of Bldg. 1, visit https://bit.ly/3U3483c and enter "MD Montgomery Co National Institutes of Health Bldg. 1."

Remember to enter your employer as "National Institutes of Health."

For more information, visit https://www.biketoworkmetrodc.org.

Cerf spoke to a packed Masur Auditorium. Attendees were also treated to an open conversation the internet evangelist had with NIH Director Dr. Monica Bertagnolli, who posed questions from NIH staff.

PHOTOS: LESLIE KOSSOFF

Cerf

CONTINUED FROM PAGE 1

heuristic programming, "which roughly means sometimes it works, sometimes it doesn't," he quipped. "If it works all the time, that's engineering. If it doesn't, that's artificial intelligence."

Computing pioneers then advanced "expert systems," or "if/then/else phrases" that would trigger each other, training programs toward a solution based on conditions that emerged.

That led to the earliest neural network, or "perceptron," which was a single-layer algorithm that could not sense correlations well, Cerf explained.

Currently in AI evolution, we are at the Neural Networks stage, he said. Large language models use what's called "generative pre-trained transformer" (GPT) technology to process natural speech, dialect, semantics and syntax.

'Unbelievably Brilliant, Equally Confusing'

The speedy developments in GPT tech have computer scientists as well as non-IT society both enthused and worried.

"Today's large language models are simultaneously unbelievably and unexpectedly

Several IT-Focused NIH'ers Have Working Lunch with Cerf

Before internet pioneer Dr. Vinton Cerf took the stage in Masur Auditorium, he met several IT-focused NIH leaders for a working lunch.

"We chatted about a variety of topics," noted one attendee, Clinical Center Senior Investigator Dr. Ronald Summers. He briefly described a few subjects that came up at the meeting, including which "aspects of AI are more likely to be incorporated into health care delivery. [Cerf] thought AI image analytics were more likely than large language models to be incorporated first."

The small group also discussed when IP version 6 will completely replace version 4. "This is pretty technical, but he seemed to enjoy this topic and talked for quite a while about it," Summers recalled.

The cadre posed questions as well.

"How can academics—I include government scientists here—innovate in the AI space, given the need for resources far beyond their (and their institutions') budgets?" Summers asked. "This has to do with the current situation where only the big companies can offer the very high salaries to attract AI talent and can purchase the huge amount of computing resources—e.g., [graphics processing units] GPUs—needed to train large language models and annotate huge datasets. [Cerf] offered to connect us with Google scientists to discuss this and also pitched Google's cloud offerings."

Time went by quickly and was well spent, as Cerf engaged the group with candor and shared personal stories.

"Vint has a witty sense of humor and we talked on a broad range of topics, from his early days of developing the internet and TCP/IP to pressing new problems such as adoption of IP6," said NIH Associate Director for Data Science Dr. Susan Gregurick, who also directs the Office of Data Science Strategy.

Before taking the stage in Masur Auditorium, Dr. Vinton Cerf (fourth from l) had a working lunch with NIH'ers (from l) Ivor D'Souza, acting director of the Center for Information Technology; Dr. Michael Chiang, director of the National Eye Institute; Dr. Susan Gregurick, NIH associate director for data science and director of the Office of Data Science Strategy; Dr. Ron Summers, senior investigator in the Imaging Biomarkers and Computer-Aided Diagnosis Laboratory at the Clinical Center; Dr. Yang Fann, director of clinical informatics at the National Institute of Neurological Disorders and Stroke; Dr. Jon McKeeby, chief information officer at the Clinical Center and chief of CC's department of clinical research informatics; and Dr. Steve Sherry, director, National Center for Biotechnology Information at the National Library of Medicine (NLM) and NLM associate director for scientific data resources.

PHOTO: DIANA GOMEZ

"We discussed AI, challenges and new opportunities, including the role of government and the opportunities of researchers and the private sector," she recounted. "He told us about his trip to Saudi Arabia and the work he is doing with their national health care initiatives to make health care available to all citizens, including those who are remote. The Saudis have an amazing program in telemedicine where devices and sensors are placed in homes and…remote clinics, and citizens engage doctors via remote conferencing platforms, like Zoom, I imagined. The hour flew fast and the meeting was rewarding."

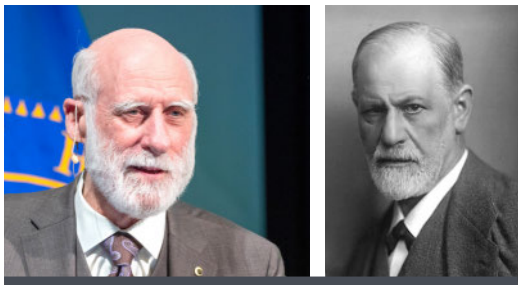
Cerf joins a long list of cultural luminaries to deliver NIH's Rall Lecture since its start in 1984.

brilliant—and equally confusing," Cerf noted, adopting a comedic impression of the late founder of psychoanalysis, Austrian physician Sigmund Freud, who he admittedly resembles physically.

"Well, what we have now are ze artificial id und ze artificial ego," Cerf joked. "What we are missing yet is ze artificial superego to control ze uncontrollable impulses of ze artificial id."

The audience applauded roundly, appreciating both the humor and the sentiment. Out-of-control AI—and the perception of its potential harms—dominates headlines about the technology these days.

"Apart from the large-language models and the hallucinations they exhibit," Cerf said, "is that they still show remarkable capability...We know there are some things it doesn't do well. That should not distort your understanding and appreciation for what might be possible here at NIH when it comes to gathering large amounts of data, understanding correlations that are exhibited by that data and then looking for the causal model that will explain what those correlations are."



During his lecture, Cerf (l) delivered a humorous impression of the late Austrian physician Sigmund Freud (r). The two resemble physically.

In advance of his talk, NIH'ers posed approximately 115 questions via online polling. After about a quarter hour in lecture mode, the internet guru transitioned to a seat on stage for an open conversation with Bertagnolli, who was armed with five of the top-voted questions.

In Sickness and in Health

She led with a surprising true statement: "A major problem with health care is that actually very, very little of it is based upon rigorous clinical data."

One of Bertagnolli's major priorities as NIH director is to provide more evidence-based medical care and to make it available to more people. She asked Cerf how AI might help.

★★★

"...You have the opportunity to make enormous progress, because you're the source of fabulous research, great data and now the potential for using computer-based tools to make your predictions even more precise."

-DR. VINTON CERF

★★★

For starters, he recommended, health care providers might consider gathering data on people when they are healthy as well as when they are sick, in order to establish a baseline wellness factor.

"If I were a doctor and my patients only came in when they have symptoms or are sick, then all my statistics would say my patients are always sick," Cerf pointed out. "One thing that is very important is to collect information about patients when they are not sick, so that I have some sense of what's normal for them. That will help me figure out if and when they have gone on some excursion away from the norm. So, instrumenting ourselves might be very beneficial for ourselves as well as medicine in general."

Huge Potential for Good

Other topics ranged from how AI can detect and weed out misinformation to ways the biomedical research community can better standardize its data for optimal sharing to Cerf's advice for scientists just beginning their careers.

"I hope you realize what an opportunity NIH has to improve the state of health care not only here in the U.S. but elsewhere with the kind of research you're doing and the attempt to exercise these powerful computing tools that are emergent," Cerf concluded. "Generally something has happened over the last 20 years that I'll call 'computational X' for every value of X you can think of—linguistics, chemistry, physics, economics—we are using computing tools increasingly to build models, test the models, to try to understand how the world works, to make predictions.

"NIH is invested heavily in trying to develop those kinds of tools," he continued, "and you have the opportunity to make enormous progress, because you're the source of fabulous research, great data and now the potential for using computer-based tools to make your predictions even more precise. If I were you, I'd be sitting here thinking, 'Boy do we have a lot of work to do and a huge amount of opportunity to do good.'"

The event was popular NIH-wide. More than 700 people requested tickets for a venue that holds about 450. In addition to the in-person packed house, close to 1,800 people watched via NIH videocast livestream. View the recording at https://videocast.nih.gov/watch=54305.

The lecture is named in honor of Dr. Joseph "Ed" Rall, who helped define NIH's modern Intramural Research Program and in the 1950s was instrumental in establishing an academic-like and culturally rich community within a government agency that was growing fast.

Since 1984, when Rall recommended adding a cultural talk to the NIH Director's Lecture series, NIH has hosted such guests as opera singer Renée Fleming in 2019 to explore music and the mind, the Dalai Lama in 2014 to address the role of science in human healing, screen and stage icon Barbra Streisand in 2018 to discuss women's heart health, and journalist Dr. Sanjay Gupta in 2015 to talk about medicine and the media.

Pelvic

CONTINUED FROM PAGE 1

can affect both men and women. While PFDs typically do not cause physical harm if untreated, they are associated with depression and anxiety and may significantly impact the individual's quality of life.

Many women likely deal with some degree of PFDs, especially if they have given birth. Aging also increases the likelihood of experiencing symptomatic PFD. The decrease in estrogen that comes with menopause may contribute to weakening and loss of strength in the pelvic floor muscles. Other risk factors for these conditions include conditions that cause excess or chronic straining, such as constipation and obesity, or extremely high-intensity workouts such as heavy weightlifting.

Dr. Donna Mazloomdoost

"Pelvic floor disorders are often dismissed as a 'normal' part of aging, but it's not something you have to live with. Treatments do exist," said Dr. Donna Mazloomdoost, a urogynecologist and medical officer with the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Gynecologic Health and Diseases Branch (GHDB). Her main research areas involve pelvic floor disorders, obstetric fistula and female genital mutilation. She started her career as an obstetrician/gynecologist and became interested in urogynecology as a subspecialty due to the large prevalence of women with PFDs she encountered in her practice.

PFDs are more likely to occur with aging, but younger women can also develop them. "There are no good estimates on the actual prevalence," Mazloomdoost lamented. "PFDs are probably more widespread [than we realize] because women may not report them due to embarrassment or beliefs that they are not treatable."

Pelvic Floor Dysfunction

Another affliction of the pelvic floor is called pelvic floor dysfunction. Women with the condition may have excessively tight pelvic floor muscles that may also contribute to other symptoms such as constipation, frequent urinary urges, pain with intercourse or pelvic pain. The muscle spasms are called levator hypertonus, and this condition is distinct from PFDs because the former causes pain, whereas PFDs are uncomfortable but not typically associated with pain.

Treatment

The first line of treatment for PFDs and dysfunction is often pelvic floor physical therapy. Pelvic floor exercises can help patients with PFD improve muscle tone and function. Pelvic floor physical therapy often focuses on pelvic muscle relaxation and retraining, or even a specific massage called myofascial release in cases of levator hypertonus. A supportive device such as a pessary can be used to treat pelvic organ prolapse (a hernia that develops in the vagina causing the pelvic organs to drop from their position and bulge into or out of the vagina). Medications can also be used to treat many of these conditions. Surgery may be beneficial for some pelvic floor conditions.

Stigma

Pelvic floor disorders and dysfunction often come with stigma. PFD symptoms such as urinary incontinence after giving birth may seem like a fact of life or may feel like a low-priority issue to a new mom. Symptoms can also be embarrassing. Patients who experience pelvic floor conditions may be reluctant or embarrassed to discuss their symptoms with their doctor. Furthermore, non-specialized gynecologists may not be trained to treat pelvic floor conditions, and a urogynecologist may not always be available in the region.

Urogynecology is a relatively new board-certified subspecialty, so patients may not even know what resources are available to them, and doctors who do not specialize in the field may not know where to refer patients.

Pelvic floor exercises during pregnancy may aid in recovery after childbirth.

PHOTO: MARIDAV/SHUTTERSTOCK

Dr. Helena Ahn

"Ending up on the right doorstep is the biggest hurdle," Mazloomdoost said. She still sees patients in addition to her NICHD work, and she said women often suffered symptoms for three to eight years before seeking treatment.

Pain Disorders

Sometimes, women can experience pelvic pain with no visible or obvious cause. The pain may intersect with pelvic floor dysfunction, but that is not always the sole cause.

Dr. Helena Ahn is a GHDB program officer who oversees grants related to gynecologic pain, including chronic pelvic pain, endometriosis-associated pain, dysmenorrhea (menstrual pain), dyspareunia (pain with intercourse) and vulvodynia (chronic pain around the vulva/vaginal opening).

A neurobiologist by training, Ahn said so much of what she learned about gynecologic pain was new and interesting to her.

"It is surprising that many women are suffering from gynecologic pain and yet we don't have much knowledge about these conditions," she noted. "Most people don't feel comfortable talking about their gynecologic pain conditions, which may delay the proper pain management or treatment."

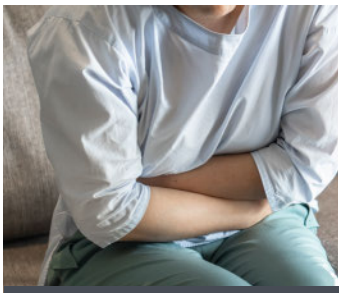
Chronic pelvic pain syndrome is estimated to affect nearly 15 percent of the general population and is associated with decreased quality of life, loss of productivity and increased health care use. Also, treatment is costly: Women with chronic pelvic pain spend roughly $881.5 million yearly in direct health care costs, and the overall cost is roughly $2 billion.

Researchers do have some idea of what contributes to chronic vulvovaginal pain, and the sources are myriad:

- injury or irritation to the nerves that supply feeling to the vulva
- an increase in nerve endings or inflammatory markers in the vulvar skin

- abnormal response of the vulvar cells to environmental factors
- changes to hormone receptors in the vulva
- genetic factors
- localized hypersensitivity to yeast or other microorganisms
- weakness or spasm of the pelvic floor muscles

GHDB aims to improve women's reproductive health by guiding and supporting gynecologic research. One of the branch's research priorities is to understand the mechanisms of chronic gynecologic pain. There is limited understanding of the prevalence, biological mechanisms and clinical risk factors responsible for the development of gynecologic pain syndromes. More vigorous basic, clinical, and translational research is needed, particularly considering the urgent need for effective and safe non-opioid options for pain management.



Chronic pelvic pain affects an estimated 15 percent of the general population.

PHOTO: CHINNAPONG/SHUTTERSTOCK

Understudied

Most grants Ahn sees are focused on pain related to menstruation or endometriosis—both worthy causes—but the lack of awareness about the most stigmatized gynecologic pain conditions leave millions of patients without adequate resources.

"Gynecologic pain is a very understudied and underfunded research area. Across NIH, gynecologic pain received far less funding in fiscal year 2022 ($6.5M) when compared to pain research ($978M), back pain ($66M) or headache ($54M)," Ahn said.

GHDB organized the NICHD Gynecologic Pain Virtual Meeting in 2022 and 2023 to bring together investigators in the field of gynecology and pain to spur interest, share ideas and discuss challenges, gaps and future directions in gynecologic pain research. Those meetings provided opportunities for investigators to network and collaborate, leading to new grant proposals.

Ahn has noticed the power of this increased awareness: "Interest in gynecologic pain is growing. The number of grant applications and awarded grants related to gynecologic pain has been increasing recently."

Knowledge Is Power

Despite this increase in interest, there is still much we don't know about what causes changes to the pelvic floor and its component structures.

"If we could understand the causes then we could better direct treatment," Mazloomdoost said.

Advocacy from both patients and practitioners is crucial, Mazloomdoost and Ahn emphasized. They are also feeling heartened by the recent White House Initiative on Women's Health Research, and Executive Order on Advancing Women's Health Research and Innovation, which aims to overhaul how the U.S. approaches and funds research on women's health.

Mazloomdoost also has a message for women who are currently experiencing pelvic floor conditions: "We've come a long way in our understanding—we have treatments now that we didn't have 20 years ago."

Perhaps most importantly, though: "Don't lose hope," she concluded. "Things often get better once the appropriate condition is diagnosed." R

Manly To Give Mahoney Lecture on Aging

BY KIM CALVIN

Dr. Jennifer Manly

Dr. Jennifer Manly, a neuropsychologist whose research is focused on structural and social mechanisms of inequalities in cognitive aging and Alzheimer's disease, will deliver the next NIH Florence Mahoney Lecture on Aging on Wednesday, May 8 at 2 p.m. ET.

Manly's presentation, "From Policies to pTau: Exposing Social and Structural Drivers of Alzheimer's Disease and Opportunities for Brain Health Justice," will take place in Lipsett Amphitheater, Bldg. 10 on NIH's main campus in Bethesda and via https://videocast.nih.gov/watch=54115. She will discuss research that establishes connections between upstream institutional and social inequalities, including those reinforced by structural racism, and downstream disparities in Alzheimer's disease and related dementias biomarkers and cognitive decline. Her research also reveals potential sources of resilience to neuropathology and forms the basis for advocating for brain health justice and developing interventions to reduce Alzheimer's and related dementias risk.

Manly is a professor at the Taub Institute for Research on Alzheimer's Disease and the Aging Brain; the G.H. Sergievsky Center; and the Columbia University Medical Center. Her team partners with the Black and Latinx communities in New York City and across the U.S. to conduct investigations of educational opportunities, socioeconomic inequality and discrimination toward understanding how these factors relate to Alzheimer's and related dementias biomarkers and cognition later in life.

A key goal of Manly's research is improving the diagnostic accuracy of neuropsychological tests when used to detect cognitive impairment and Alzheimer's among African-American and Hispanic older adults. This work also clarifies the independent influences of language, acculturation, educational experiences, racial socialization and socioeconomic status on cognitive test performance, with the goal of understanding more about the relationship between culture and cognition.

Manly earned her bachelor's degree from the University of California, Berkeley, in 1991, and a Ph.D. in clinical psychology with a specialty in neuropsychology from the University of California, San Diego/San Diego State University Joint Doctoral Program in 1996.

In 1998, she completed her postdoctoral research and joined the faculty at Columbia University, where she has risen through the ranks, serving as an assistant professor and associate professor. She was promoted to her current position in 2018.

Manly has received multiple awards in recognition of her research accomplishments, including the Early Career Award from the National Academy of Neuropsychology in 2006 and election to the National Academy of Medicine in 2021, along with numerous mentorship awards. She is an NIH grant recipient, currently serves on the NIH Council of Councils and is a past member of the National Institute on Aging (NIA) National Advisory Council on Aging.

This year marks the 50th anniversary of NIA, which Florence Stephenson Mahoney (1899-2002) helped establish through her advocacy. Named in her honor 37 years ago, Mahoney lectures are sponsored by NIA.

‘GROWING THE PIE’

National Academies Committee Plans for Expanding Women’s Health Research at NIH

BY AMBER SNYDER

The Committee on the Assessment of NIH Research on Women’s Health has taken on the task of identifying areas of greatest potential for women’s health research at NIH. Part of the National Academies of Science, Engineering and Medicine, the committee aims to identify gaps in research across all NIH institutes and centers (ICs) that, if filled, would help improve understanding of women’s health. The organization is a frequent advisor to NIH, providing independent and objective advice on a variety of topics.

Lindsey Miltenberger

The assessment committee has met frequently since the end of November 2023, and expects to issue its final report late this year. The group hosted a series of meetings to seek input from researchers, health care practitioners, NIH representatives, the public and other interested parties.

NIH representatives from the National Institute of General Medical Sciences (NIGMS), National Institute on Minority Health and Health Disparities, Sex and Gender Minority Research Office (SGMRO), Center for Scientific Review and Office of Extramural Research (OER) attended the January meeting.

“It’s difficult to choose even a handful of areas because women’s health research as a whole is underfunded and underprioritized,” said Lindsey Miltenberger, chief advocacy officer of the Society for Women’s Health Research (SWHR), at a recent meeting of the committee. She cited data from an analysis conducted by Dr. Arthur Mirin in the *Journal of Women’s Health:*

In nearly three-quarters of cases where a disease mostly affects one gender, funding patterns favor males; either the disease affects women more but is underfunded in respect to disease burden, or the disorder affects men more but is overfunded in respect to disease burden.

Heather Guidone

The disparity between actual funding and that which is commensurate with burden is almost twice as large for diseases that favor males versus females.

The disparities have major consequences for how women are diagnosed and treated for many conditions, Mirin stated. His study found that some of the most under-funded diseases are female-dominated—chronic fatigue syndrome, migraine, headaches, anorexia and endometriosis—equating to fewer researchers having the ability to acquire the funding to study these conditions.

Common solutions raised at public meetings held by the committee include finding ways to bolster early-career women researchers, who may be more likely to study female-specific conditions. Panel members also discussed ways to make clinical trials more accessible to women and increase the inclusion of female animals and cells in basic and preclinical research.

Many presenters also mentioned the need to meet people and communities where they are to facilitate better understanding of their needs.

NIGMS, through its Institutional Development Award (IDeA) program, has joined forces with the Office of Women’s Health Research (ORWH) and other NIH components to fund administrative supplements on research related to women’s health. The Building Interdisciplinary Research Careers in Women’s Health program, for example, has supported more than 750 women’s health researchers, the majority of whom are women who have competed successfully for research funding after the program.

Dr. Michele McGuirl

“The enthusiasm for these supplements led to another partnership with the ORWH to promote new IDeA Centers of Biomedical Research Excellence (COBREs) that emphasize women’s health,” explained Dr. Michele McGuirl, acting director of NIGMS’s Division for Research Capacity Building. “These Centers aim to build a critical mass of investigators who can compete effectively for independent research funding in the COBRE’s scientific area. We’re delighted that two COBREs in women’s health have been awarded this year.”

Dr. Karen Parker

Another area of concern for committee representatives is health outcomes for minoritized women, who often face unique challenges in receiving proper care.

“The dearth of research focusing on sexual and gender minority (SGM) women, the lack of adequate data collection and less access to resources are a few of the unique barriers and inequities that SGM women face,” explained SGMRO Director Dr. Karen Parker. “Fostering inclusion in the workforce, increasing diverse representation of women in research, expanding data collection and increasing precision in language concerning sex and gender are just some of the many ways that SGMRO works to advance women’s health research.”

NIH’s Sex as a Biological Variable (SABV) policy is also a frequent topic at committee meetings.

Established in 2016, the SABV policy set the expectation that researchers would account for the possible role biological sex could play in vertebrate animal and human studies. Meeting participants asked whether the policy goes far enough and how it can be enforced.

In addition to defining these considerations, the committee plans to assess the appropriate amount of funding needed to address the gaps in women’s health research at NIH. In the January meeting, OER’s Division of Scientific Categorization and Analysis provided context on the intricacies of the NIH budget and how research funding is allocated.

The general sentiment from expert presentations at public meetings held by the committee thus far seems to be that more funding overall is needed, rather than dividing current funds differently.

All understudied conditions are equally deserving of a “slice of the pie” when it comes to funding, reasoned Heather Guidone, program director at the Center for Endometriosis Care and a speaker in a stakeholder perspective session at a committee meeting early this year. She shared the words of Dr. Shyam Bishen of the World Economic Forum: “The solution is not to divide more slices of one pie—it is to make more pie.”

To learn more about the committee, visit https://bit.ly/3xERekD.

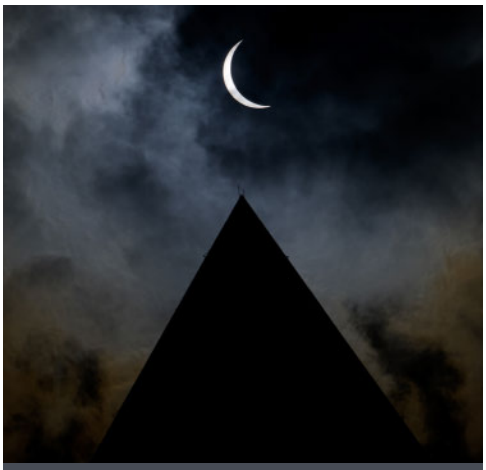
NIH'ers Gather to Watch Solar Eclipse

Hundreds of employees and visitors on NIH's Bethesda campus tilted their heads skyward to watch the solar eclipse.

On Apr. 8, a total solar eclipse swept across North America, passing over Mexico, 15 states and Canada. Despite being hundreds of miles from the path of totality, NIH'ers still saw the moon partially block out the sun.

In the Washington, D.C. area, the moon began to cross the sun at 2:04 p.m. By 3:20 p.m., the moon obscured 87% of the sun at maximum eclipse. For the next 4 minutes and 28 seconds, the moon partially covered the sun. At 4:32 p.m., it ended.

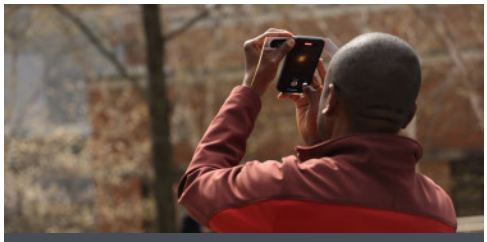
The eclipse was the first since 2017 (https://go.nih.gov/9pncXbI). The next total solar eclipse that may be seen in the contiguous United States will occur on Aug. 23, 2044, and be visible in Montana, North Dakota and South Dakota.



In the Washington, D.C., area, the eclipse peaked at 87% coverage of the sun. Above, the moon is seen passing in front of the sun, with the top of the Washington Monument in silhouette. **PHOTO: BILL INGALLS/NASA**
Below, people watch the moon's movement from outside the Clinical Center's south entrance. **PHOTO: CHIA-CHI CHARLIE CHANG**

Zoe Kaegi, a first-year postbac in Dr. Susan Amara's Laboratory of Molecular and Cellular Neurobiology in NIMH, shows off her pinhole projector made from a lab supplies box.
PHOTO: KIRSTEN SNYDER

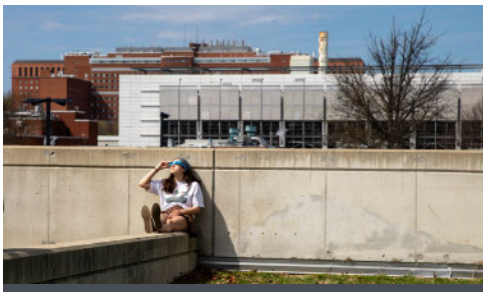
Above, folks look at the eclipse through a cardboard box pinhole projector. Below, Dr. Nina Schor (second from l), NIH deputy director for intramural research, views the partial eclipse through a pinhole projector made from a sheet of paper. **PHOTOS: ERIC BOCK**



A man photographs the eclipse using solar glasses with his iPhone.
PHOTO: CHIA-CHI CHARLIE CHANG

Employees gather outside the NIH Library to watch the spectacle through protective glasses.
PHOTO: CHIA-CHI CHARLIE CHANG

Dr. Andrew Bower (l), NEI clinical and translational imaging section, brings the solar eclipse into focus on a computer-mounted telescope. **PHOTO: DUSTIN HAYS/NEI**



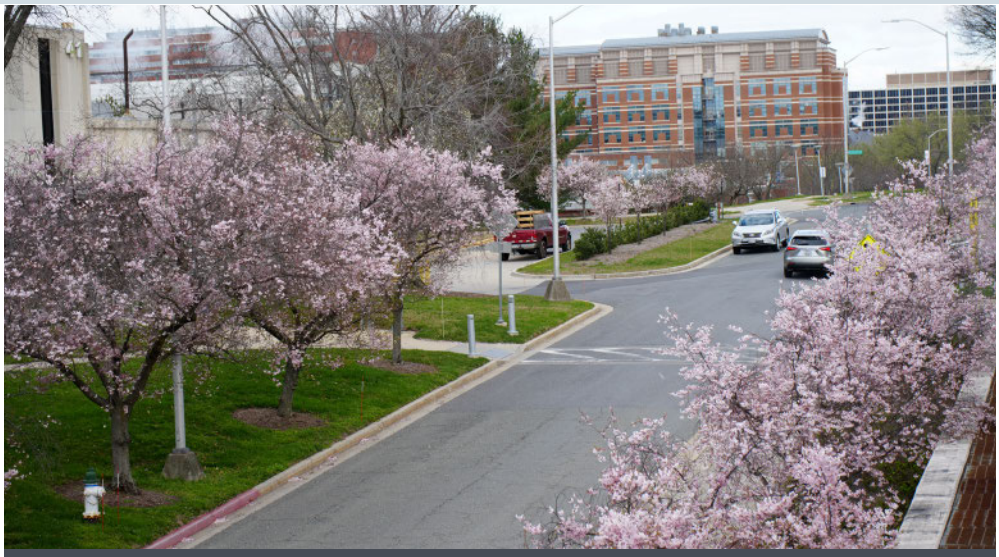
Above, an observer watches the eclipse on the south side of the NIH campus. Below, Annette Kaminaka of NEI's clinical and translational imaging section views the event via a pinhole camera. **PHOTOS: DUSTIN HAYS/NEI**

NIH's Cherry Blossoms Reach Peak Bloom

PHOTOS: ERIC BOCK

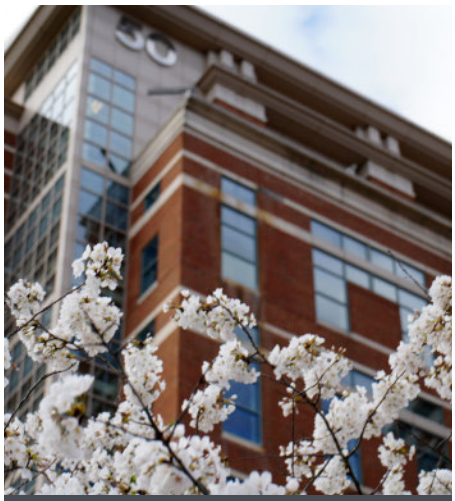
The cherry blossoms on NIH's Bethesda campus reached peak bloom toward the end of March.

Each spring, the blossoms typically reach peak in late March or early April. Full maturity varies depending on weather conditions. Once peak occurs, the blossoms remain on the trees for about a week. Wind, rain or cooler temperatures can cause the petals to fall off faster.



Cherry blossoms line the road leading to MLP-7.

Above, cherry blossoms in front of Bldg. 1. Below, blooms near the Clinical Center's north entrance



Above, blossoms next to Bldg. 50, also known as the Louis Stokes Laboratories. Below, cherry blossoms near Bldg. 15H, one of the "Officer's Quarters" on NIH's main campus