

NCATS Aims to Transform Rare Disease Research

BY ERIC BOCK

For patients with a rare disease, it all starts with a diagnosis.

“Getting an accurate diagnosis early, easily and expeditiously is a critical step in bringing the best possible care to people with rare diseases,” said NCATS acting



NCATS acting director
Dr. Joni Rutter

director Dr. Joni Rutter during NIH’s annual observance of Rare Disease Day.

Far too often, however, patients with a rare disease face a “diagnostic odyssey” that lasts, on average, 7 years, Rutter noted. It includes misdiagnoses, inappropriate care and unnecessary tests and procedures.

There are more than 7,000 rare diseases and only 5 percent of them have a treatment, she said. To speed up discoveries, the NCATS-led Platform Vector Gene Therapy (PaVe-GT) seeks to make it easier to start clinical trials by using the same gene delivery system and



NIH lit up Building 38A in Rare Disease Day colors.

PHOTO: NCATS

manufacturing methods for multiple rare disease gene therapies.

NIH worked with industry to launch the

SEE RARE DISEASE, PAGE 4

THE WEST AND THE REST

Historian Draws Lessons from Past Pandemics

BY DANA TALESNIK

When a disease event becomes a pandemic, looking at it through a lens of science informs leaders to gauge the threat—transmission rate, illness severity, mortality—and organize a response to mitigate its effects.

For centuries, though, a system of imbalanced international disease controls and power politics have shaped pandemic response, argued Dr. Alexandre White, who is mining NLM



Dr. Alexandre White

SEE PANDEMICS, PAGE 6

STOMACH BUGS

Scientists Reveal the Good, Bad and Ugly of *H. Pylori*

BY AMBER SNYDER



Dr. Martin Blaser

Ever heard that stomach ulcers are caused by stress? Turns out it’s a lot more complicated than that.

Stomach (or peptic) ulcers are just one component of a complex web of interactions between the human body and

one of the thousands of bacterial species that make up our microbiomes (the community of bacterial species that live in and on our bodies). *Helicobacter pylori*, the bacterium

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Pediatric asthma care study reports disparities. See Digest on p. 11.

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NIH Chief Officer for Scientific Workforce Diversity (COSWD) Strategic Plan

COSWD Releases Strategic Plan

NIH's chief officer for scientific workforce diversity (COSWD) team has released its Strategic Plan for Fiscal Years 2022-2026. The plan outlines a bold vision for future efforts and renews the team's charge to lead the science of scientific workforce diversity, using evidence-based approaches to catalyze cultures of inclusive excellence.

Over the next 5 years COSWD activities will promote diversity, equity, inclusion and accessibility in the biomedical research enterprise through 3 goals:

- Build the evidence
- Disseminate the evidence
- Act on the evidence

Visit <https://go.usa.gov/xuxrR> to explore the strategic plan.



Dr. Keith Muller and Dr. Deborah Glueck

Next 'Mind the Gap' Webinar Features Muller, Glueck

The Office of Disease Prevention (ODP) will host a Methods: Mind the Gap webinar with Dr. Keith Muller and Dr. Deborah Glueck on Friday, Apr. 29 at 1 p.m. ET.

Planning a reproducible study requires selecting a sample size expected to ensure appropriate statistical power. Advances in statistical methods and free point and click software have made it easy to select a sample size for clustered and longitudinal designs with linear mixed models.



Musical Mix in the CRC Atrium

In the Clinical Research Center atrium on Mar. 24, University of Maryland professors and alumni performed classic jazz, Brazilian classics and a little funk. Musicians shown above include (from l) Danny Villanueva on percussion, Joey Antico on drums, Gerry Kunkel on guitar, John Previti on bass and Jon Ozmet on piano.

PHOTO: DEBBIE ACCAME

The software, a suite of training modules and reference materials are freely available online. The software interface and training materials are aimed at health scientists, and have been validated in face-to-face and online courses.

Dr. Keith Muller and Dr. Deborah Glueck will discuss what the software and training cover, what they do not cover and what they hope to add.

Muller is a biostatistician specializing in the design and analysis of multilevel and longitudinal research. He is a fellow of the American Statistical Association. He earned bachelor's and master's degrees in psychology from Bradley University, as well as a doctorate in quantitative psychology and a master's degree in theoretical statistics from the University of North Carolina at Chapel Hill.

Glueck is the senior biostatistician at the Lifecourse Epidemiology of Adiposity & Diabetes Center at the Colorado School of Public Health and professor of pediatrics at the University of Colorado Denver School of Medicine. She has a career-long focus on power and sample size for multilevel and longitudinal studies and the analysis of longitudinal epidemiological cohort studies and randomized controlled clinical trials.

Registration is required. Register at: <https://go.usa.gov/xuxra>. The webinar will be recorded and available on the ODP website within approximately 2 weeks.

The Methods: Mind the Gap webinar series explores research design, measurement, intervention, data analysis and other methods of interest in prevention science. For more information, visit: <https://go.usa.gov/xuxrT>.

Credit Union Re-Establishes Some Full Service on Main Campus

With the NIH workforce returning to a partial onsite work schedule, the NIH Federal Credit Union (NIHFCU) will be re-establishing Monday-Friday (9 a.m.-4 p.m.) full service branch access on the main campus starting the week of Apr. 18.

- Clinical Center: Monday-Wednesday (mask required)
- Bldg. 31: Thursday-Friday

The credit union thanks you for following its social-distancing procedures to support a safe environment for all visitors, employees and the NIH community.

To learn more about all that is new at the NIHFCU, including financial products and services, remote banking solutions and other branch hours, visit nihfcu.org or stop by any branch.

Collins To Deliver 2022 Chanock Lecture

Former NIAID principal investigator and section chief Dr. Peter L. Collins returns to NIH to present the 2022 NIAID Robert M. Chanock Memorial Lecture. The talk, titled “A Memoir of Research on Respiratory Syncytial Virus (RSV) and Related Viruses: Baby Steps,” will take place on Tuesday, Apr. 26, at 9 a.m.



Dr. Peter L. Collins will give the next Chanock Lecture on Apr. 26.

The in-person lecture will be by invitation only; other interested members of the NIH community are welcome to join remotely at: <https://nih.zoomgov.com/j/1611000456>.

The lecture honors the late virologist Dr. Robert M. Chanock, who worked at NIAID for more than 50 years, including more than 3 decades as chief of the Laboratory of Infectious Diseases (LID), and was a pioneer of translational research in infectious diseases.

Among other accomplishments, Chanock identified

multiple viruses that cause disease in people, including RSV, and made major contributions to their characterization and control. For example, he conceived of and led the development of a monoclonal antibody to prevent RSV disease in high-risk children.

RSV is a leading viral cause of serious pediatric respiratory illness worldwide, causing an

estimated 21.6 to 50.3 million cases of lower respiratory illness, 2.7 to 3.8 million hospitalizations, and 94,600 to 149,400 deaths globally each year in children under age 5. RSV also is an important cause of morbidity and mortality in the elderly.

Characterization of RSV and the development of a pediatric RSV vaccine were major activities of Chanock’s laboratory and have continued in LID

to this day. These efforts have been impeded by the difficulty of working with this virus and the challenges of developing vaccines for respiratory viruses in infants. However, LID investigators have made considerable progress. One example is the monoclonal antibody noted above, which has had extensive and successful clinical use. Also, several promising live, attenuated RSV vaccine candidates are in clinical studies being conducted in collaboration with industrial partners.

Collins’s contributions to these efforts include the molecular characterization of RSV and the use of cutting-edge molecular techniques and information to make the improved, well-defined vaccine candidates now in clinical trials.

Collins began working with RSV in 1981 and joined Chanock’s laboratory in 1984. He was chief of the RNA viruses section in LID from 2010 until his retirement in 2019. In his lecture, he will discuss some of the milestones in basic and translational studies of RSV and related viruses. **R**

AANHPI HERITAGE MONTH

Research Conference To Focus on Asian American, Native Hawaiian, Pacific Islander Health

The NIH Asian American, Native Hawaiian and Pacific Islander Health Scientific Interest Group (NIH AANHPI-HSIG) will host the inaugural Annual NIH AA and NHPI Health Research Conference on May 4-5 to celebrate AANHPI Heritage Month, highlight AANHPI research achievements and assess research needs.

The main theme of the conference is “Mechanism and Translational Research to Improve Health and Therapeutic Outcomes for AA and NHPI Populations.”

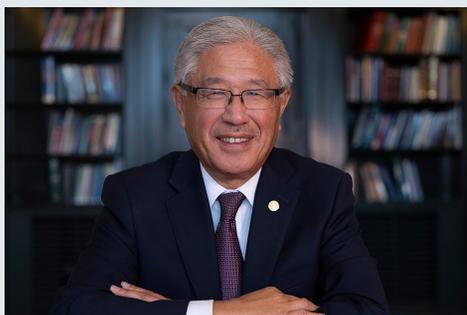
NIMHD director Dr. Eliseo Pérez-

Stable; Krystal Ka’ai, executive director of the White House Initiative on Asian Americans, Native Hawaiians and Pacific Islanders; UNITE co-chair Dr. Marie Bernard; and Dr. Katrina Goddard, director of NCI’s

Division of Cancer Control and Population Sciences, will give opening remarks. Dr. Victor Dzau, president of the National Academy of Medicine, and Dr. Howard Koh of the Harvard T.H. Chan School of Public Health will be the keynote speakers. NEI director Dr. Michael Chiang and NINR director Dr. Shannon Zenk will join the final summary and panel discussion on May 5.

Information about career development for NIH staff will also be available. Find the agenda and register for the 2-day virtual conference, which is free and open to the public, at: <https://go.usa.gov/xuxCB>.

Email questions to Dr. Dan Xi, chair of NIH AANHPI-HSIG, at: xida@mail.nih.gov.



Dr. Victor Dzau (above) and Dr. Howard Koh (r) will be keynote speakers at the conference.



ON THE COVER: *Two adult fruit flies (Drosophila)*

IMAGE: MDI BIOLOGICAL LABORATORY

The NIH Record

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National Institutes of Health
Turning Discovery Into Health

Rare Disease

CONTINUED FROM PAGE 1

Bespoke Gene Therapy Consortium, which is dedicated to making gene therapy a reality for people with genetic diseases affecting populations too small to be viable from a commercial perspective. Additionally, the NIH Common Fund's Somatic Cell Genome Editing Program is working to improve approaches to help reduce the burden of diseases caused by genetic changes.

"These are all programs that are poised to transform the pipeline for gene-targeted



Rutter discusses programs in the pipeline for rare disease research.

therapies," Rutter said. "They will bring hope to the 80 percent of rare diseases that are caused by a single-gene mutation."

All communities must benefit from new diagnostics and therapeutics. "We also have



to address the inequities in rare diseases in rural communities and communities of color. That means access to newborn screening, care, treatments—that goes with it," she said.

Rutter's mother, Dorothy, was one of the 30 million Americans with a rare disease. Dorothy had primary myelofibrosis, a condition characterized by the buildup of scar tissue in the bone marrow. It took her 15 years to get a diagnosis and, when she was diagnosed, there were no treatments. Eventually, there were clinical trial options, but they were 800 miles away.

"I am dedicated to finding ways to

improve all of these factors," Rutter concluded. "I know I am not alone in that sentiment and that's what gives me hope."

Rare Disease Day 2022 featured updates from researchers, stories from patients and their families and panel discussions.

"NIH is proud to be a longtime supporter of rare disease research," said NIH acting director Dr. Larry Tabak. "Evidence of our commitment can be seen across our research portfolio. It's reflected, for example, in the depth and breadth of ongoing research to understand genetic diseases."

Just one example of that commitment is the Rare Diseases Clinical Research

Rare Diseases Affect Patients as Well as Caregivers

Rare diseases affect more than the individual with the disease, said Dr. Margaret Bevens, during a Rare Disease Day session on caregiver resilience.

"They affect many others, including family members, and often parents, who serve as caregivers," said Bevens, director of the Office of Research Nursing in NHLBI's Office of the Clinical Director.

Caregivers are not paid and don't receive any formal training. They give of themselves unconditionally to those they love to make a difference, she said.

They report higher levels of anxiety, depression, fatigue and loneliness. Oftentimes, they have to change their daily lives and restrict leisure activities. One study of parents with a child with a rare disease found they have a slightly lower quality of life compared to parents with healthy children.

"Caregiving is a chronic stressor," said Bevens. "It is a complex and complicated experience that includes multiple competing priorities."

There are many positive aspects of caregiving, such as finding meaning and being connected with people we love, said Bevens. However, "caring for another person, no matter how much you love them, is heavy."

To build resilience, they must learn how to balance caring for another and one's own emotional, spiritual and physical health.

"There are many professional interventions that your providers can refer you for, which can help support you and build resilience," she said.

Additionally, there are everyday activities caregivers can do to cultivate balance, she said. They can, for example, find a trusted support person to share their feelings; improve communication with family, friends and providers; delegate responsibilities to others; exercise and pursue physical activity; get fresh air and explore nature; and make time to be mindful.

"As you prioritize your self-care, remember the acronym, REST—relax, eat healthy and stay active, sleep and take care of yourself," Bevens concluded.

Find resources for caregivers on the Clinical Center's website at: <https://cc.nih.gov/wecare>.



Caregivers must also take care of themselves, notes Dr. Margaret Bevens. "I'm here today to make a universal statement of permission for all caregivers of those with rare disease: participate in everyday self-care activities."



NIH acting director Dr. Larry Tabak discusses tangible progress NIH has made in rare disease research.

Network: 10 institutes and centers, 166 patient advocacy groups, 20 consortia and 1 coordinating center make up the network.

“Through the network consortia, physician scientists and their multidisciplinary teams work together with patient organizations as active research partners to study 181 rare diseases across the nation,” Tabak said.

Gaucher disease is one of the rare diseases being studied by the network, he noted. The disease is a group of inherited metabolic diseases in which harmful amounts of fatty materials accumulate in various cells and tissues in the body. There are several different types of Gaucher disease. They range in severity from lethal to asymptomatic.

Because of the network, multiple institutes and centers can support research that seeks to learn more about Gaucher disease. “A broad scope is needed to truly gain a better understanding of the disorder,” Tabak said.

There are many important lessons rare disease researchers can learn from the Covid-19 pandemic—progress in telemedicine, remote capture and seamless scientific sharing. “Patients, families and practitioners should long benefit from these advances,” he said.

Both Rutter and Tabak thanked former director of the Office of Rare Diseases Research at NCATS Dr. Anne Pariser, who recently retired from federal service, for her contributions to rare disease research.

To watch an archived video of the day’s presentations, visit:

<https://videocast.nih.gov/watch=44155>. 

‘ENVIRONMENTAL IMPACTS’

NIEHS To Hold Virtual Workshop on Women’s Health, Apr. 27-28

NIEHS will host a virtual workshop, “Environmental Impacts on Women’s Health Disparities and Reproductive Health,” on Wednesday, Apr. 27 from 9 a.m. to 5 p.m. and Thursday, Apr. 28, from 9 a.m. to 1 p.m. ET.

A post-workshop networking session will be held from 1:15-2:15 p.m. on Thursday to allow workshop participants to follow up with speakers and NIEHS staff and scientists.

The workshop will examine health outcomes related to women and those assigned female at birth, and reproductive environmental health disparities (EHD).

The event aims to:

- Raise awareness of the impact of structural racism, racial inequities and the environment on adverse women’s reproductive health outcomes often observed in U.S. health disparity populations.
- Create an opportunity for NIEHS staff to learn more from the community about the current status of EHD and women’s reproductive health and community outreach efforts.
- Identify knowledge gaps in EHD and women’s reproductive health that can be developed into NIEHS scientific focus areas.



Workshop sessions will include speaker presentations and interactive panel discussions that feature national and local leaders in environmental health disparities research and women’s reproductive health. The event is organized by the NIEHS Environmental Health Disparities and Environmental Justice Faculty.

The virtual workshop is free and open to the public. Pre-registration is required. Register now at: <https://tools.niehs.nih.gov/conference/ehdworkshop2022/>.

Individuals with disabilities who need sign language interpreters and/or reasonable accommodation to participate in this event should contact Dr. Darlene Dixon at darlene.dixon@nih.gov or (984) 287-3848.

Pandemics

CONTINUED FROM PAGE 1

archives to illuminate this history. He discussed some of his findings at a recent NLM History of Medicine lecture.

“The ongoing global pandemic of Covid-19 perhaps has laid bare the politics of global relations work at the heart of pandemic governance,” said White, assistant professor, Johns Hopkins University and associate director of its Center for Medical Humanities and Social Medicine.

“It is much clearer now,” he said, “that an epidemic, far from signifying solely a biological threat to life, is also an economic and political phenomenon, which produces cascading, conjoined effects including xenophobia, nationalist fervor, racial oppression as well as the exposure of the health effects of racism and its dark violent disparities.”

The history of international infectious disease control, said White, has largely involved powerful imperial North American and European nations elevating themselves as models of hygiene and sanitation, threatened by diseases entering from less sanitary nations. For centuries, imperial powers have driven the narrative, developing assumptions and courses of action based on global disease threats that endanger health, travel and trade.

“We can see the ways in which these rooted and continuing social imbalances operate in epidemics, especially while we’re living through them,” said White, “but also by looking at the history of human responses to epidemic threat.”

By the late 19th century, most of Europe and North America developed sanitation systems that helped control food and waterborne diseases in urban areas. And, as the west learned to control or eradicate such insect-borne diseases as yellow fever and malaria, attention turned toward chronic disease and population health.

“The eradication of smallpox, the mostly successful eradication of polio and the development of vaccines against childhood diseases like measles, mumps and

rubella have made these formerly devastating illnesses in the west cosmopolitan centers a concern only if there’s significant lack of vaccination,” said White, “or if anti-vaccination discourses take hold.”

By the 1980s, optimism abounded that perhaps the era of global infectious disease was over. Then the HIV/AIDS pandemic arrived, killing tens of millions while highlighting health inequalities, unequal access to resources and at times apathy.

Before the Covid-19 pandemic struck in 2020, many leaders in the west presumed technological and medical advances made the developed world immune to novel infec-

practices of a bygone era, wholly alien from the sanitized spaces of modern hospitals and cosmopolitan streets,” he said. “Epidemics of disease disproportionately having greater effects outside of the overdeveloped west than within highlight, perhaps, a myth whose cracks are emerging today under Covid-19.”

That myth, he said, contends that sanitary controls and biomedical intervention separate the west from those suffering from infectious disease throughout the rest of the world.

To elucidate, White coined the term “epidemic Orientalism,” a twist on the premise of the 1978 book *Orientalism* by

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“We can see the ways in which these rooted and continuing social imbalances operate in epidemics, especially while we’re living through them.”

-DR. ALEXANDRE WHITE

• • •

tious disease. When the latest wave of Ebola hit West Africa in 2014, it was contained in the region.

“In places far away from the epicenter of the epidemic,” said White, “we watched as victims of Ebola died lonely deaths, far away from their loved ones, to be buried under intense sanitary controls.” The prolonged epidemic was blamed on local traditions and ignorance of science, “pathologized as the markers of backwards people and unhealthy behavior.”

Such practices as social distancing and quarantine “were seen as scrambling

Edward Said. This colonizing and polarizing worldview, rooted in an outlook of western superiority, White explained, has dominated epidemic responses, regulations and controls for centuries.

“The heightened scrutiny and bias against non-Europeans who were blamed for spreading disease historically resulted in aggressive, racist and xenophobic responses carried out in the name of health controls,” he said.

Back in 1901, for example, an epidemic of bubonic plague in then British-ruled South Africa resulted in the forced removal of most





In 1968, Surgeon General William Stewart posed with Rebecca Ansah Asamoah, recipient of the 25-millionth smallpox vaccination. Smallpox remains the only infectious disease eradicated worldwide.

PHOTO COURTESY NLM

of Cape Town's Black African population to a racially segregated quarantine camp. This act, noted White, was a precursor to racially segregated townships during apartheid.

Similar scrutiny was foisted upon Muslims traveling from India through the Persian Gulf into western Europe during the Hajj in the 19th century. Muslim pilgrims were perceived as a particular threat for spreading cholera. Sea lane closures risked leaving tens of thousands of Muslims stranded in the Arabian desert without food, water or shelter.

"Rather than focusing upon eradicating disease at the source or eradicating its causes," said White, "the focus of control turned to its prevention of transfer to Europe."

Today, the Covid-19 pandemic has exposed anti-Chinese sentiment, which has reared its ugly head before in U.S. pandemic response.

"Public health actors in the late 18th and 19th centuries believed a variety of diseases, including parasitic diseases, were more common among Chinese immigrants," said White, and used this rationale as the basis for exclusion, especially at western ports of entry.

When bubonic plague spread in Honolulu in 1900, city administrators quarantined Chinatown, excluding White American-owned businesses adjacent to the quarantine site.

"The quarantine posed considerable hardships on [the Chinese population] within, limiting employment, movement and access to supplies," said White.

This form of epidemic Orientalism was reflected in 19th-century legislation, said White. The Page Act of 1875 banned immigration of Chinese women to the U.S., on the perception that they were sex traffickers carrying virulent diseases. And the

Chinese Exclusion Act of 1882 banned all Chinese immigration to the U.S. Such laws paved the way for exclusionary immigration laws against Mexicans, Central and South Americans and East Europeans.

"The Covid pandemic exposes the terrifying nearness of the 19th century—its violence, its pandemics and everyday loss of life," said White.

"This idea of a West against the rest of the world framework needs to be fundamentally challenged in future infectious disease controls and regulations...for us to develop more equitable, effective and responsive pandemic [policies]." **B**

Virtual Postbac Poster Day Scheduled, Apr. 26-28

NIH Virtual Postbaccalaureate Poster Day 2022 will take place on Apr. 26-28. The program agenda will be available on the event website below.

Poster Day provides an opportunity for postbacs to share the research they have been conducting at NIH and at the same time develop their scientific communication and networking skills.

Posters will be reviewed and judged by teams composed of graduate students, postdocs and staff scientists/clinicians. Authors of the top 20 percent will receive a letter acknowledging their accomplishment.

For more information, visit: <https://go.usa.gov/xuxrf>.



NIH senior investigator Dr. Peter Basser

NICHD's Basser To Deliver Annual Chen 'Tech Transfer' Talk, Apr. 29

NIH senior investigator Dr. Peter Basser will deliver the 15th annual Philip S. Chen Jr. Distinguished Lecture on Innovation and Technology Transfer on Friday, Apr. 29 at 10 a.m. ET via <https://videocast.nih.gov/watch=44974>.

The title of his talk is "Using Water Migration to Probe Brain Structure and Architecture."

Basser heads NICHD's section on quantitative imaging and tissue sciences and serves as associate scientific director of the Division of Translational Imaging and Genomic Integrity. He has the unique distinction of being the only current NIH principal investigator elected to the National Academy of Engineering.

The Chen Lecture was established in 2006 by the NIH deputy director for intramural research and the Office of Technology Transfer (OTT) on the occasion of Chen's retirement after more than 40 years of service to NIH.

Chen established OTT to implement the provisions of the Federal Technology Transfer Act. He formulated the guiding principles upon which technology transfer functions today, including the creation of CRADAs or Cooperative Research and Development Agreements.

Basser studies relationships between function and structure in living tissues, particularly how their microstructure, hierarchical organization, composition and material properties affect their function or dysfunction. To do this, he and his lab have developed several non-invasive imaging methods that allow them to observe various transport phenomena in tissue, which provide a link between structure and function. The most widely used method is diffusion tensor magnetic resonance imaging, or DTI. Basser is its principal inventor.

For details about the Chen Lecture and its history, visit: <https://go.usa.gov/xuxrf>.

Stomach

CONTINUED FROM PAGE 1

that resides in the nearly inhospitable acidic environment that is the human stomach, has only recently begun to be understood.

Dr. Barry Marshall of the University of Western Australia and Dr. Martin Blaser of Rutgers University gave a joint presentation in the Demystifying Medicine series titled “The Split Personality of *Helicobacter Pylori*.”

“The only good *Helicobacter pylori* is a dead [one]” is the philosophy of many gastroenterologists, Blaser said. Marshall and his colleague Dr. Robin Warren identified the bacteria’s association with gastritis (inflammation of the stomach lining), and peptic ulcers in 1982.

The earliest recorded observation of the spiral-shaped bacteria was 100 years earlier in 1892, but they had never been successfully cultured outside the stomach before and thus no one paid much attention to them. Many researchers didn’t believe Marshall and Warren’s findings at first—including Blaser.

“Never publish a paper that shows results in 100 percent of patients because no one will believe it,” Marshall laughed.

It was also a commonly held belief that the human stomach was too acidic for microbial life. The research community came around eventually, and Marshall and Warren shared the 2005 Nobel Prize in Physiology or Medicine for their work with *H. pylori*.

Marshall and other researchers found that most people with duodenal and gastric ulcers also have *H. pylori*. Bismuth

subsalicylate (the active ingredient in Pepto-Bismol) turned out to be one drug already in existence that killed helicobacter. Bismuth, behaving as an antibiotic, along with other common antibiotics were found to quash *H. pylori* in ulcer patients, thus allowing the ulcer to heal and largely preventing relapse.

Blaser and colleagues showed that *H. pylori* was the most important risk factor for the most common type of stomach cancer (non-cardia), which affects the lower portions of the stomach. According to Blaser, helicobacter-positive individuals may have upwards of a 6-fold greater risk of developing non-cardia gastric cancer.

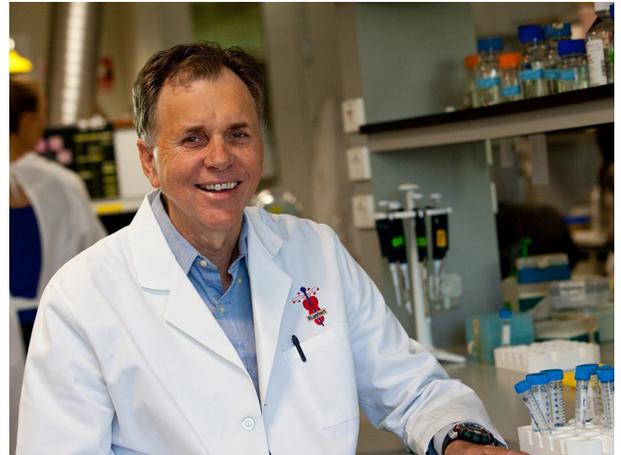
‘Split Personality?’

Blaser, a physician and microbiologist, became interested in the relationship between helicobacter and humans. Was it truly all bad, or were there hidden benefits to the human host?

Today, approximately half of the global population carries *H. pylori*. Most infected individuals do not develop ulcers or gastric cancer and may not have any adverse symptoms at all. Blaser proposed that the bacteria actually had a “split personality”—that it caused some deleterious effects but also some beneficial ones.

Blaser and others obtained helicobacter samples from patients around the world and sequenced their DNA with fascinating results: modern helicobacter strains can

be traced to ancestral ones that flourished thousands of years ago. This ordination is consistent with the idea that humans have been carrying helicobacter since before the out-of-Africa event, which was 58,000 years ago, he revealed. “As humans diverged around the world, so did their helicobacter... [and it probably] has been in humans and our ancestors since before



Marshall of the University of Western Australia in his lab

we were humans.”

By definition, that makes *H. pylori* a co-evolved colonizing persistent microbe. But, Blaser asked, what happens to the host when that microbe is lost?

As Blaser studied *H. pylori*, he noticed an interesting trend. Since the bacteria had first been measured in human populations in the early 1900s, its prevalence has decreased steadily and significantly. In 1915, it was found in about 60 percent of Americans. By the 1990s, that percentage had fallen to less than 10. The reason for the decline is suspected to be improved sanitation, chlorinated water and widespread usage of antibiotics.

Nitty Gritty of Acidity

The incidence of asthma and other allergic responses has increased in the post-war period, Blaser said, and researchers have identified a link between asthma and a condition called GERD (gastroesophageal reflux disease), in which stomach acid flows into the esophagus.

The human stomach has a pH of 1.5-3.5. This acidity aids in digestion by breaking down food, and also kills pathogens such as viruses and bacteria. Most bacteria cannot survive in pH less than 3. So, how does *H. pylori* survive in this hostile environment?

It produces an enzyme called urease, Marshall said. Urea is a compound found in stomach acid, and the urease enzyme made by *H. pylori* breaks down urea and forms ammonia, an alkaline (less acidic) substance.

“The helicobacter form a less acidic buffer around them with urease,” Marshall explained. “Normal people have urea in their



Dr. Barry Marshall (top, l) and Dr. Martin Blaser (bottom) gave a joint virtual presentation in the Demystifying Medicine series hosted by Dr. Win Arias (top, r).

stomach acid, but people with *H. pylori* don't because the bacteria is using it up."

Less stomach acid could potentially be helpful in conditions like acid reflux and GERD. Damage from stomach acid in the esophagus and upper stomach (gastric cardia) is a risk factor for adenocarcinomas, so scientists speculate that reduced stomach acid may diminish acid damage and the likelihood of esophageal and gastric cardia cancers. Blaser provided evidence that *H. pylori* is bad for the lower stomach and duodenum, but protective for the upper stomach and esophagus.

Physicians, Heal Themselves

Both Marshall and Blaser share a willingness to include themselves in their research. In order to test his initial hypothesis that helicobacter causes gastritis, Marshall drank two petri dishes of the bacteria.

"It was tasteless, thankfully," he laughed. He developed gastritis 10 days later and ultimately took antibiotics to rid himself of the bacteria.

Blaser made an important discovery: cytotoxin-associated gene A (*cagA*), by studying antibodies in his own blood that identified this important protein in the *H.*

pylori strain he was carrying in his stomach.

The presence of this gene allows researchers to divide *H. pylori* populations into *cagA+* and *cagA-* strains. *CagA* produces a toxin that alters the structure of stomach lining cells and allows helicobacter to attach more easily. The toxin can cause chronic inflammation over time. Studies have shown that *cagA+* strains are associated with an increased risk in non-cardia gastric cancer, and reduced risk of gastric cardia and esophageal adenocarcinoma.

However, a study from Blaser's group in New York showed that people with *cagA+* helicobacter were less likely to develop asthma or developed it later in life, and their other independent blinded studies confirmed these findings. The bacteria may offer some protection from infections—individuals with *H. pylori* had a stronger immune response to a live oral typhoid vaccine than those without.

H. pylori is also known to regulate ghrelin, the "hunger hormone." In people with helicobacter populations, ghrelin was high before eating and fell after a meal, while individuals without helicobacter still had higher ghrelin levels after eating.

So, "is the only good helicobacter *pylori*

a dead helicobacter *pylori*?" Blaser asked. "I don't think so. [It] is an ancestral member of the human microbiota. Its disappearance has consequences, both good and bad. That is the future of medicine."

He and Marshall discussed a future where people could be infected with *H. pylori* at an early age to reap the bacteria's benefits, and then treated for the infection later in life before complications could take effect. Both agreed it was a radical idea, but not out of the question.

"We've changed the ecology of the stomach," Blaser said, "[but] the logic is leading back to that."

The archived lecture can be found at <https://videocast.nih.gov/watch=44343>. 

BUILD YOUR CAREER, SHAPE YOUR FUTURE

OITE's 15th Annual Career Symposium To Be Virtual

The NIH Office of Intramural Training & Education invites all NIH graduate students and postdoctoral trainees, both basic scientists and clinicians, to participate in the 15th annual NIH Career Symposium being held virtually on May 11-13.

The symposium provides an opportunity for fellows and graduate students to learn about scientific career options and to explore factors that lead to career success.

This multi-day virtual program will include networking sessions highlighting career opportunities available to biomedical scientists. Panel sessions cover academic, government, industry and non-profit career paths. Speakers will provide insights into their careers—what their current job entails, its pluses and minuses and how they got there.

For more information and registration visit: <https://www.training.nih.gov/>.



Join our chat on **BOOSTING** your community

April 20, 2022
2:00 - 3:00 p.m. ET

COVID-19 Gamechangers: Trusted Messengers Giving Communities a Boost!

More Activities to Boost Your Community

April is National Minority Health Month! This year's theme "Give Your Community a Boost" highlights the continued importance of Covid-19 vaccination, including boosters, and supports the Surgeon General's efforts to combat health misinformation.

Join NIMHD for a Twitter chat co-hosted with the HHS Office of Minority Health, "Covid-19 Gamechangers: Trusted Messengers Giving Communities a Boost!" on Wednesday, Apr. 20 from 2-3 p.m. ET. Use #NMHM22Chat to participate in the English chat with @NIMHD and the Spanish chat with @OMH Espanol.

Also, check out the website below for other features and activities—download social media messages, Zoom backgrounds and customizable graphics and play Minority Health Bingo in English and Loteria in Spanish.

For the latest NMHM updates, visit <https://nimhd.nih.gov/programs/edu-training/nmhm/>.

VOLUNTEERS

Epstein-Barr Vaccine Study Recruits

NIAID researchers are seeking to enroll healthy volunteers ages 18-29 living in the Washington, D.C., Maryland and Virginia area in an investigational Epstein-Barr virus (EBV) vaccine clinical trial. If you are eligible, consider joining to help research on EBV—the most common cause of infectious mononucleosis (mono) and a virus associated with some cancers. For more information, contact the Clinical Center Office of Patient Recruitment at (866) 444-2214 (TTY users dial 711) or ccopr@nih.gov. Refer to study #21-I-0005. Online: <https://go.usa.gov/xsYK5>.

Hazra Named NICHD Division Director

Dr. Rohan Hazra has been appointed director of the NICHD Division of Extramural Research. He had been serving as the acting director of DER since February 2020, just before the Covid-19 pandemic began. During this challenging time, he excelled at keeping NICHD's extramural program focused and productive.



Dr. Rohan Hazra

"Dr. Hazra brings a wealth of experience as a researcher, clinical trialist and science administrator to his role as DER director," said NICHD director Dr. Diana Bianchi. "I am confident that his leadership will help us continue and even accelerate progress toward our institute's scientific and public health goals."

Prior to being appointed DER acting director, Hazra was chief of DER's Maternal and Pediatric Infectious Disease Branch. In this role, he provided scientific leadership for domestic and international research, research training and career development programs related to the epidemiology, diagnosis, pathogenesis, transmission, treatment and prevention of HIV and other selected pathogens in infants, children, adolescents and pregnant people.

DER staff develop, implement and coordinate multidisciplinary research activities to advance NICHD's mission of understanding human development, improving reproductive health, enhancing the lives of children and adolescents and optimizing abilities for all. The division's portfolio encompasses biological, behavioral and clinical research related to conception and pregnancy, normal and abnormal development in childhood, reproductive health and population dynamics across the lifespan.

Hazra's research interests include studying the long-term impact of HIV and its treatment on children, adolescents and young adults with perinatally acquired HIV. He also is involved in clinical trials evaluating new antiretroviral medications and treatment strategies for children with HIV, especially those living in resource-limited countries.

Hazra received his bachelor's degree in biology from Yale University and his M.D. from Johns Hopkins University School of Medicine. He completed a pediatric residency and pediatric infectious disease fellowship at Children's Hospital in Boston.

Prior to joining NICHD in 2007, he conducted clinical studies in pediatric HIV in the NCI's intramural program. Hazra is certified by the American Board of Pediatrics in both pediatrics and pediatric infectious diseases.

Collins, Fauci Receive Richardson Public Service Honor

Former NIH director Dr. Francis Collins, who currently serves as a senior investigator in the intramural program of the National Human Genome Research Institute and was recently appointed acting science advisor to President Joe Biden, and Dr. Anthony



ELR Prize committee chair Michael Rogers (l) presents award virtually to Dr. Francis Collins (c) and Dr. Anthony Fauci.

Fauci, director of the National Institute of Allergy and Infectious Diseases and chief medical advisor to the President, received the 2022 Elliot L. Richardson Prize for Excellence in Public Service. This prize is presented annually by the National Academy of Public Administration. Both NIH'ers were also inducted as honorary members of the academy.

The award recognizes individuals for extraordinary public service, in the tradition of the late Richardson, who served as a beacon of integrity and commitment to public service. Richardson served in four Cabinet-level positions in the federal government, including secretary of health, education and welfare; secretary of defense; attorney general; and secretary of commerce.

According to its bylaws, the prize is awarded to individuals "possessing the public service virtues Richardson exemplified and [who] have demonstrated achievement significantly advancing the public good, and long-term dedication to public service." Honorees additionally have shown "generosity of spirit, thoughtfulness in the pursuit of excellence in government, courage and integrity."

NCI's Fraser Mourned

Capt. Mary C. Fraser, former clinical research nurse and commissioned officer in the Public Health Service in NCI's Division of Cancer Epidemiology and Genetics (DCEG), died Mar. 5, after a long illness. She served NCI for nearly three decades working with cancer-prone families before her retirement in 2018.

Fraser had a long and distinguished career as one of the first clinical research nurse specialists in what became DCEG. She pioneered the central role of nurses in long-term studies of families at increased risk of cancers, focusing on melanoma-prone families. She was essential in developing the clinical aspects of enrolling and maintaining contact with high-risk families, many of whom, especially in the early days, were not familiar with medical research processes.

In addition to her recognized expertise in familial melanoma, she also was a nationally acknowledged expert in the long-term effects of cancer therapy, both systemic chemotherapy and radiation therapy.

Fraser is survived by her husband, children and grandchildren.

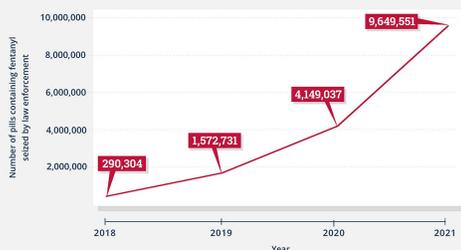


Capt. Mary C. Fraser

Research Shows Dangerous, Growing Trend of Illicit Fentanyl Use

Law enforcement seizures of pills containing illicit fentanyl increased dramatically since 2018, according to a new NIDA-funded study published in *Drug and Alcohol Dependence*.

Number of Pills Containing Fentanyl Seized by Law Enforcement in the United States, 2018 – 2021



The number of pills containing fentanyl seized by law enforcement increased dramatically in the U.S. between 2018–2021.

PHOTO: NIDA

The number of individual pills seized increased nearly 50-fold from the first quarter of 2018 to the last quarter of 2021, and the proportion of pills to total seizures more than doubled by the end of 2021.

The latest CDC data shows the U.S. hit a record high in overdose deaths, estimating that nearly 106,000 people died from drug overdoses in the 12-month period

ending in October 2021. This rise is largely driven by illicit fentanyl and other synthetic opioids.

Illicit fentanyl is highly potent, cheaply made and easily transported, making it a profitable narcotic. While people may seek out illicit fentanyl intentionally, many people are not aware the drug they are using—including heroin, cocaine, methamphetamine or benzodiazepines—may actually be fentanyl, or was contaminated with it. Because fentanyl is about 50 times more potent than heroin and a lethal dose may be as small as 2 mg., using a drug laced with fentanyl greatly increases overdose risk.

To ascertain the extent that fentanyl is found in counterfeit pills, a research team led by Dr. Joseph Palamar of the NYU Grossman School of Medicine and co-investigator on the NIDA-funded National Drug Early-Warning System, analyzed data on drug seizures by law enforcement. The data were collected from the High Intensity Drug Trafficking Areas (HIDTA) program in which the Drug Enforcement Administration and CDC play an active role.

“We absolutely need more harm-reduction strategies, such as naloxone distribution and fentanyl test strips, as well as widespread education about the risk of pills that are not coming from a pharmacy,” said Palamar. “The immediate message here is that pills illegally obtained can contain fentanyl.”

HIDTA data are made available quarterly, allowing evaluation in almost real time. Analyzing these data can therefore help identify trends in availability of illicit substances and act as an early-warning system to shift public health education or interventional resources more quickly.

Disparities Found in Use of Pediatric Asthma Care

Black children with asthma accessed community health centers (CHCs) less than White children, while Latino children (who prefer to speak either English or Spanish) were more likely to visit CHCs for acute, chronic and preventive care overall, according to a new, large NIMHD study published in *Annals of Family Medicine*.

The pattern of low clinic usage by Black children was accompanied by more frequent emergency department visits compared to the other groups. The difference in use at the CHC level suggests there are other factors beyond affordability influencing disparities in health care utilization.

Led by researchers at the Oregon Health & Science University, Portland, the study compared acute asthma care visits within CHCs, and the equivalent

use within hospital emergency departments by race, ethnicity and language. The 7-year observational study conducted across 18 states using the electronic health records of 41,276 children with asthma found 54 percent of Black children had fewer than 2 visits annually, while for White and Spanish-prefering Latino children, it was 49.2 percent and 30.1 percent, respectively. The minimum standard of care for children with asthma is two visits annually.



A large, NIMHD-funded study compared acute asthma care visits within community health centers.

MICHAEL JUNG/SHUTTERSTOCK

Additionally, researchers examined how acute care use may reflect social factors across various domains, including aspects of poverty. Researchers found that most children in the study experienced a wealth gap, but Black children did so more often than others. These children may have been affected by greater financial instability, the inability of guardians to take work leave or fill prescriptions leading to lower primary care usage and increased exacerbations that could require emergency care.

Other research has shown that in equally segregated and socially deprived neighborhoods, immigrants have better health outcomes (including higher primary care usage) than non-immigrant Black people do. This contrast suggests the effects of long-term structural racism may have influenced the findings in this study.

Medication Helps Protect Insulin Production in Type 1 Diabetes

A drug approved to treat high blood pressure, called verapamil, was found protective in people with type 1 diabetes. Over the 2-year study, the protective effects lasted as long as people took the drug, reducing the amount of insulin treatment required.

The study, funded in part by NIDDK, was published in *Nature Communications*.

Type 1 diabetes is usually diagnosed in children and young adults, although it can appear at any age. In people who have the disease, the immune system attacks and destroys beta cells in the pancreas that make insulin—a hormone that controls the amount of glucose in the bloodstream.

Injections of insulin can prevent blood glucose from rising to dangerous levels, but treatment comes with health risks and high costs.

In previous research, a team from the University of Alabama at Birmingham found that verapamil protected beta cells and reversed diabetes in mouse models of type 1 diabetes. In a small clinical trial, the drug improved the functioning of beta cells in people recently diagnosed with the disease. But it was unclear how and how long the drug worked.

The team analyzed blood samples from 5 of the study participants who received verapamil and 5 who received a placebo. They found that levels of 53 proteins changed in the blood after a year of verapamil treatment. One, called chromogranin A (CHGA), stood out. It changed the most over time, dropping substantially in people who received the drug.

CHGA is found in beta cells and suspected to play a role in the immune system attack that causes type 1 diabetes. CHGA blood levels were elevated in people with type 1 diabetes compared to healthy people.

Data from larger, ongoing studies of verapamil will be needed to confirm these results.—adapted from *NIH Research Matters*

A TREE GROWS IN ASIA

McCurdy To Discuss Kratom, Apr. 25

Dr. Christopher McCurdy, a medicinal chemist and behavioral pharmacologist at the University of Florida (UF), will give a virtual lecture, “Can a Controversial Tree Help End the Opioid Crisis?” on Monday, Apr. 25 from 1 to 2 p.m. ET. The event is part of NCCIH’s Integrative Medicine Research Lecture Series.



Medicinal chemist Dr. Christopher McCurdy

Kratom (*Mitragyna speciosa* Korth) is a tree in the coffee family that is indigenous to Southeast Asia. Its leaves are the source of a Thai traditional drug, kratom, with unique pharmacologic actions—e.g., both stimulant actions and depressant ones. Kratom has been used traditionally in its region of origin as an opioid substitute and a treatment for addiction. Little was known scientifically, however, about this plant.

Recently, human case reports have increased in the literature from its use in the United States, and the U.S. Drug Enforcement Administration has listed kratom as a “drug and chemical of concern.”

McCurdy will discuss the traditional medicinal use of this botanical, examples of current pharmacologic studies and his team’s studies in rodent models. Kratom’s differing uses, availability and preparation around the world will also be explored. The potential of kratom and its major alkaloid, mitragynine, to treat opioid withdrawal is a key focus.

McCurdy is the Frank A. Duckworth eminent scholar chair in drug research and development and a professor of medical chemistry at UF, and the director of the UF Translational Drug Development Core. His research focuses on the design, synthesis and development of drugs to treat pain and drug abuse. McCurdy holds a Ph.D. in medicinal chemistry from the University of Georgia.

No registration is required for the lecture and all interested persons are welcome. The event will be streamed live and archived on NIH VideoCast and NCCIH Facebook.

More information is at <https://bit.ly/CRMcCurdy>.



PHOTO: CHIA-CHI CHARLIE CHANG

Construction of VRC Addition Begins

Construction has commenced on the NIAID Vaccine Research Center’s Bldg. 40A, a tower adjacent to the current Bldg. 40 at the intersection of South Drive and Convent Drive on NIH’s main campus. For the latest information on navigating around construction, see <https://traffic.nih.gov/Pages/default.aspx>.

The new facility (shown below in an artist’s rendering) will be 158,000 square feet with 5 working floors and a ground level. Floors 2 to 5 will have large and small meeting rooms, laboratory space, tissue culture rooms and designated equipment rooms. Staff will be able to walk between the two buildings on each level and collaborate with each other with ease.

The new space will support VRC’s mission to facilitate development of effective vaccines for human diseases. The expansion also will create new opportunities for trainees and early-career investigators to further contribute to a broad array of research programs.

