OUTOOO K WAShington University in St. Louis School of Medicine

unprecedented times Courageous Medicine



Racism is a Public Health Crisis #White Coats For Black Lives

Led by its students, the Washington **University Medical Campus community** participated in a White Coats for Black Lives demonstration. Racial inequity leads to gaps in insurance coverage, lower access to services and poor health out<u>comes. In</u> Missouri, African Americans with COVID-19 are dying at a rate more than 2.5 times their share of the population. See page 16 for more about student response.





On an ICU window, caregivers note the times a patient with COVID-19 was turned face down. The simple, noninvasive technique of proning boosts blood oxygen saturation levels among COVID-19 patients, potentially delaying or eliminatin



COVER A nurse comforts a patient with COVID-19 in a Barnes-Jewish Hospital ICU. Because of the high infection risk, loved ones often must communicate with patients via phone or iPad. See more about front-line clinical care on page 22.

FEATURES

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Danforth, MD, served Washington University for more than 65 years. See page 46.

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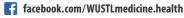
From cardiologist to chancellor, William H.

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Neuroscience research hub

Construction progresses on largest project in medical school's history

he School of Medicine's eastern border will look strikingly different in 2023, when the neuroscience research building — 11 stories tall and 609,000 square feet — is complete. The building project, the largest in the medical school's history, will span almost a block in the 200-acre Cortex Innovation Community, one of the fastest-growing business, innovation and technology hubs in the U.S.

The project will connect the campus core to the Cortex Innovation Community and bring together interdisciplinary neuroscience research and innovation at the medical school.

Initially, 5½ floors of the building will house 100 research teams in laboratory space. Those teams will come from a wide array of disciplines, including the neurology, neuroscience, neurosurgery, psychiatry and anesthesiology departments.

University School of Medicine

The building is the first facility on the Medical Campus to feature research "neighborhoods" on each floor to spur collaboration. The neighborhoods will be organized around research themes including addiction, neurodegeneration, sleep and circadian rhythm, synapse and circuits, and neurogenomics and neurogenetics — that bring people together with common interests.

The school has a long history as one of the world's foremost centers for neuroscience research, including as a leading institution in the study of Alzheimer's disease. David H. Perlmutter, MD, executive vice chancellor for medical affairs, the George and Carol Bauer Dean of the School of Medicine, and the Spencer T. and Ann W. Olin Distinguished Professor, said the new facility will open

No in the

the door to bold new research initiatives and partnerships.

"Understanding the brain is key to addressing some of the most devastating afflictions that affect mankind," Perlmutter said. "So many of us have been touched by the inexorable decline of our loved ones due to diseases and conditions such as Alzheimer's and Parkinson's, brain trauma, glioblastoma and severe mental illness."

Additional shell space could be built out later for another 45 research teams. The building will feature a large seminar room on the first floor and a coffee shop with an outdoor terrace on the third floor. The project will include a 1,839-space parking garage, a pedestrian link connecting the St. Louis Children's Hospital garage and a separate utility plant.



The 2020 Nobel Prize in Physiology or Medicine was awarded Oct. 5 to three scientists for the discovery of hepatitis C virus. One of those scientists — virologist Charles M. Rice, PhD — conducted his seminal work while on the School of Medicine faculty from 1986 to 2000. Rice, now at Rockefeller University in New York City, was awarded the prize along with Harvey J. Alter, MD, of the National Institutes of Health (NIH) and Michael Houghton, PhD, of the University of Alberta in Canada.

In announcing the prize, the Nobel Assembly said the hepatitis C discovery had "made possible blood tests and new medicines that have saved millions of lives." The discovery is a landmark achievement in the ongoing battle against viral diseases, the Nobel Assembly said.



Rice remains an adjunct professor in the Department of Molecular Microbiology at the School of Medicine.

He described his surprise in getting a phone call at 4:30 a.m. notifying him of the award. When the phone rang, Rice assumed it was a prank call and let it go. But when the phone rang a second time, he

Charles Rice, PhD

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answered. "... There was a voice with a Swedish accent on the phone When he mentioned that my friends and colleagues Harvey Alter and Mike Houghton were also being recognized with this prize, it started to sink in that it might actually be real," Rice said.

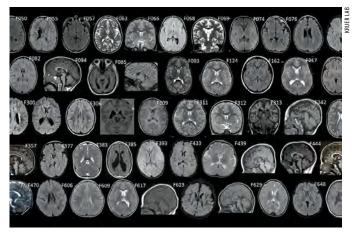
Before the discovery of hepatitis C virus, physicians and researchers were concerned by unexplained cases of chronic hepatitis that developed years or decades after blood transfusions. At the time, only two viruses were known to cause hepatitis, and both had been ruled out. Hepatitis A virus does not spread through the blood, and while hepatitis B virus does, a blood test and vaccine had been developed to prevent infection.

Alter demonstrated that an unknown virus was a common cause of unexplained blood-borne chronic hepatitis, and Houghton isolated the genome of the new virus, which was named hepatitis C virus. Rice provided the critical final evidence showing that infection with hepatitis C virus alone could cause hepatitis.

To learn more about stories in Pulse, go to **medicine.wustl.edu/news**

The new building will sit

at 4370 Duncan Ave.



MRI brain scans from patients with cerebral palsy. For many patients with the disorder, doctors can't pinpoint the cause.

New research shows genetic basis for cerebral palsy

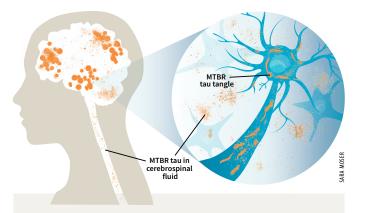
The causes of cerebral palsy have long been debated and often are attributed to in utero infections, premature birth, or brain injury to the baby near or during delivery, usually from a lack of oxygen. But many young children diagnosed with cerebral palsy have not experienced such events.

Now, a new study led by researchers at the School of Medicine, the University of Arizona College of Medicine in Phoenix and Yale University has identified mutations in single genes that can be responsible for at least some cerebral palsy cases. The study indicates that many of the mutations occur randomly and are not inherited from a child's parents. The research is part of the International Cerebral Palsy Genomics Consortium, a global effort to understand genetic causes of cerebral palsy.

The scientists were able to show that introducing mutations of the same genes into fruit flies caused the insects to have movement difficulties that resemble those common in people with cerebral palsy, a common neurodevelopmental disorder.

To better understand genetic contributions to cerebral palsy, the scientists sequenced the entire protein-coding portion of the genomes from 250 participants — cerebral palsy patients and both parents — seeking mutations that could play causal roles in cerebral palsy.

"This international collaboration allowed us to conduct the largest genetic analysis of cerebral palsy patients and their parents to date," said Sheng Chih (Peter) Jin, PhD, an assistant professor of genetics at Washington University. "What is exciting about uncovering new genetic causes of cerebral palsy is the potential for the future development of therapies for these patients."



Novel tau fragments in the spinal fluid, which track with tangles of tau protein in the brain, could lead to earlier diagnosis of Alzheimer's disease.

Novel tau fragments found in spinal fluid

A novel form of an Alzheimer's protein found in cerebrospinal fluid indicates what stage of the disease a person is in, and tracks with tangles of tau protein in the brain, according to a School of Medicine study. Tau tangles are thought to be toxic to neurons, and their spread through the brain foretells the death of brain tissue and cognitive decline. Tangles appear as the early, asymptomatic stage of Alzheimer's develops into the symptomatic stage.

The discovery of so-called microtubule binding region tau (MTBR tau) could lead to a way to diagnose people before they have symptoms or when their symptoms are still mild and easily misdiagnosed. It also could accelerate efforts to find treatments for the devastating disease, by providing a relatively simple way to gauge whether an experimental treatment slows or stops the spread of toxic tangles.

The study is published in the journal Brain.

Tau tangles can be detected by positron emission tomography (PET) brain scans, but brain scans are time-consuming, expensive and not available everywhere. Senior author Randall J. Bateman, MD, the Charles F. and Joanne Knight Distinguished Professor of Neurology, and first author Kanta Horie, PhD, a visiting scientist in Bateman's lab, realized that specific MTBR tau species were enriched in the brains of people with Alzheimer's disease, and that measuring levels of the species in the cerebrospinal fluid might be a way to gauge how broadly the toxic tangles have spread through the brain.

Previous researchers using antibodies against tau had failed to detect MTBR tau in the cerebrospinal fluid. But Horie and colleagues developed a method based on using chemicals to purify tau out of a solution, followed by mass spectrometry.

Clinic treats emerging psychotic disorders

The first signs of mental illness involving psychosis — the experience of having hallucinations, delusions or intrusive, disturbing thoughts — often appear during the teen years. Emerging evidence suggests early intervention may help such adolescents avoid serious problems as they get older, such as educational and family disruption.

A new clinic now is providing free treatment to adolescents and young adults, ages 13 to 25, who may be at high risk, in the early stages or who have been diagnosed with a psychotic illness within the prior three years.

Treatment is

provided regardless of whether the patient has insurance, courtesy of grant support from the St. Louis County Children's Service Fund, The Foundation for Barnes-Jewish Hospital and the



St. Louis Children's Hospital Foundation. If medications are needed, however, there are costs associated with those.

Psychosis is a symptom of psychiatric illnesses such as schizophrenia and some forms of bipolar disorder. Such illnesses affect an estimated 3% of the U.S. population, according to Daniel Mamah, MD, director of the new clinic, called the Washington Early Recognition Center (WERC).

"There is a real need to help young patients and their families because psychotic disorders tend to get worse over time, especially if untreated," Mamah said. "The aim of this clinic is to get patients into treatment as early as possible, providing them with interventions such as individual psychotherapy, family therapy and medication."

The clinic, at 4444 Forest Park Ave., is the only one of its kind in the St. Louis region. During the COVID-19 outbreak, visits are being conducted using telemedicine.

For more information, call 314-362-6952 or visit werc.wustl.edu.



The Office of Medical Public Affairs has a new podcast, "Show Me the Science," that features the latest in groundbreaking research, clinical care and education at Washington University. Listen and subscribe on Apple Podcasts, Spotify, or wherever you listen to podcasts.

Diabetes in mice cured rapidly

chool of Medicine researchers have converted human stem cells into insulin-producing cells and infused them in mice — resulting in controlled blood sugar levels and diabetes being functionally cured for nine months.

"These mice had very severe diabetes with blood sugar readings of more than 500 milligrams per deciliter of blood — levels that could be fatal for a person — and when we gave the mice the insulin-secreting cells, within two weeks their blood glucose levels had returned to normal and stayed that way for many months," said principal investigator Jeffrey R. Millman, PhD, an assistant professor of medicine and of biomedical engineering.

Several years ago, the same researchers discovered how to convert human stem cells into pancreatic beta cells that make insulin.

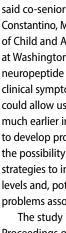
When such cells encounter blood sugar, they secrete insulin. Still, previous work has had its limitations and had not effectively controlled diabetes in mice. Now, a new technique targeting the cells' internal scaffolding, called the cytoskeleton, can more efficiently convert human stem cells into insulinproducing cells that more effectively control blood sugar. The findings were published in Nature Biotechnology. "A common problem when you're trying to transform a human stem cell into an insulin-producing beta cell — or a neuron or a heart cell — is that you also produce other cells that you don't want," Millman said. "In the case of beta cells, we might get

other types of pancreas cells or liver cells."

Potential biomarker for autism identified

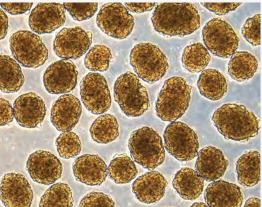
esearchers at the School of Medicine and Stanford University have identified a biomarker in newborns that may signal autism spectrum disorder months or even years before troubling symptoms develop and such diagnoses typically are made.

The researchers found that babies diagnosed with autism later in childhood had in their cerebrospinal fluid, as infants, abnormally low levels of a neuropeptide associated with the disorder.



"Autism currently is diagnosed behaviorally, mainly in children ages 2 to 4 years old," said co-senior investigator John N. Constantino, MD, director of the Division of Child and Adolescent Psychiatry at Washington University. "This neuropeptide biomarker long predates clinical symptoms, and if confirmed, it could allow us to begin interventions much earlier in children who will go on to develop problems, further opening the possibility of pharmaceutical strategies to increase neuropeptide levels and, potentially, to prevent some problems associated with autism." The study is published in the Proceedings of the National Academy of Sciences.

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Clusters of human insulin-secreting beta cells, as seen under a microscope. Jeffrey R. Millman, PhD, and his team produced these cells from stem cells.

Using the new technique, Millman's team found that far fewer off-target cells were produced while the beta cells that were made had improved function.

For this study, the researchers examined cerebrospinal fluid samples collected from 913 feverish newborns cared for at St. Louis Children's Hospital two decades ago. At the time of collection, the cerebrospinal fluid was examined for markers of meningitis but was found to be negative. The leftover fluid was saved and stored.

The scientists determined that babies whose samples had very low levels of the neuropeptide were significantly more likely to be diagnosed with autism later in childhood. Levels of the neuropeptide — arginine vasopressin — already are suspected to be lower in children with autism.

Variations in arginine vasopressin and oxytocin, another hormone, have been associated with autism spectrum disorder, but this study offers the first evidence that levels of one of the hormones are abnormal so early in life. The researchers are planning a larger study to see whether the findings can be replicated.



Timothy M. Miller, MD, PhD, (left) talks with instructor Kathleen Schoch, PhD, in his lab (prior to the COVID-19 pandemic).

Drug looks promising for genetic form of ALS

An experimental drug for a rare, inherited form of amyotrophic lateral sclerosis (ALS) has shown promise in a phase 1/phase 2 clinical trial conducted at the School of Medicine, Massachusetts General Hospital in Boston and other sites around the world and sponsored by the pharmaceutical company Biogen Inc. The trial indicated that the experimental drug tofersen shows evidence of safety that warrants further investigation and lowers levels of a disease-causing protein in people with a type of amyotrophic lateral sclerosis, or ALS, caused by mutations in the gene *SOD1*.

The study results, published in The New England Journal of Medicine, have led to a phase 3 clinical trial.

"ALS is a devastating, incurable illness," said principal investigator Timothy M. Miller, MD, PhD, the David Clayson Professor of Neurology at Washington University and director of the ALS Center at the School of Medicine. "While this investigational drug is aimed at only a small percentage of people with ALS, the same approach — blocking the production of specific proteins at the root of the illness — may help people with other forms of the illness."

Few people survive more than five years after diagnosis, and existing treatments are only modestly effective at slowing the pace of the disease.

Tofersen is an antisense oligonucleotide, which is a DNA-based molecule that interferes with the genetic instructions for building proteins. The molecule is designed to block production of the SOD1 protein.

Eli Lilly acquires startup company

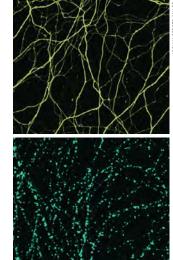
Pharmaceutical maker Eli Lilly and Company has purchased Disarm Therapeutics, a startup biotechnology firm founded by School of Medicine researchers Jeffrey Milbrandt, MD, PhD, and Aaron DiAntonio, MD, PhD.

Based on research from the Milbrandt and DiAntonio

labs, the startup company was developing drugs to block or slow axonal degeneration, a common problem across numerous neurological disorders.

"Disarm Therapeutics had reached the point in the drug development process where we either needed to raise much more funding ourselves or work with a pharmaceutical company with the infrastructure already in place to take this technology to the next level," said Milbrandt, the James S. McDonnell Professor, head of the Department of Genetics, and executive director of the McDonnell Genome Institute at the School of Medicine.

Lilly made the acquisition,



Nerve axons that are healthy (top) and degenerated (bottom).

with an upfront payment of \$135 million. If future development, regulatory and commercial milestones are met, Disarm investors may be eligible for up to \$1.2 billion in additional payments.

"The Office of Technology Management and the entrepreneurial support available to our researchers have been key to the success of Disarm," said David H. Perlmutter, MD, executive vice chancellor for medical affairs and the George and Carol Bauer Dean of the School of Medicine, "and we are enormously proud that this exciting research program at Washington University has reached the next milestone in the journey to FDA-approved drugs that help patients with devastating neurological disorders."

Milbrandt, DiAntonio — the Alan A. and Edith L. Wolff Professor of Developmental Biology — and their colleagues have demonstrated that injured or diseased axons initiate a self-destruction program. Blocking this program provides a way to stop axonal loss, a discovery that has shown therapeutic promise.





Opeolu M. Adeoye, MD, a noted leader and physician-scientist whose research focuses on improving outcomes for patients who have suffered strokes or other brain injuries, has been named **head of the newly established Department of Emergency Medicine.** He also will become the inaugural BJC HealthCare Distinguished Professor

of Emergency Medicine. Adeoye comes from the University of Cincinnati College of Medicine, where he is a professor of emergency medicine and of neurosurgery, and vice chair for research in the Department of Emergency Medicine. He also co-directs the Greater Cincinnati/Northern Kentucky Stroke Team.

The transition to the Department of Emergency Medicine from a division was driven to address the growing complexity of a specialty that treats patients needing immediate care for often life-threatening conditions.



Deanna M. Barch, PhD, an expert in cognitive and language deficits in psychological disorders, and Randall J. Bateman, MD, a leading Alzheimer's disease researcher, have been elected to the National Academy of Medicine, a part of the National Academy of Sciences.

Barch, is professor and chair of the Department of Psychological and Brain Sciences in Arts & Sciences and the Gregory B. Couch Professor of Psychiatry and professor of radiology. She was recognized for helping to identify neural and psychological mechanisms that give rise to the symptoms of psychosis and other forms of mental illness that contribute significantly to disability.

The National Academy of Medicine selected Bateman for his work in discovering the causes of Alzheimer's disease, developing the first highly specific blood test for Alzheimer's and initiating the first Alzheimer's prevention trial. Bateman is the Charles F. and Joanne Knight Distinguished Professor of Neurology.



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Lynda Heaney has been named vice chancellor for medical advancement at the School of Medicine. She works closely with Pamella A. Henson, executive vice chancellor for university advancement, and David H. Perlmutter, MD, executive vice chancellor for medical affairs and the George and Carol Bauer Dean of the School of Medicine, to develop an

even more robust organizational structure and new energy to propel philanthropic support for the medical school's strategic plan. Heaney joins Washington University from Duke Health Development and Alumni Affairs, where she was assistant vice president for principal and transformational gifts.

Winter 2020-21



Dineo Khabele, MD, gynecologic oncologist, noted for her expertise in ovarian cancer research and treatment, has been named head of the Department of Obstetrics and Gynecology. She also is the Mitchell and Elaine Yanow Professor of Obstetrics and Gynecology. Khabele previously worked at the University of Kansas School of Medicine, where she was a

professor of obstetrics and gynecology and of cancer biology, director of the Division of Gynecological Oncology and vice chair for research in the Department of Obstetrics and Gynecology.



Dave Pagliarini, PhD, whose studies of the so-called "powerhouses of the cell" have shed light on a set of rare but devastating diseases, has been named a BJC Investigator. He is joining the Department of Cell Biology and Physiology and has secondary appointments in the biochemistry and genetics departments.

Pagliarini previously served as an associate professor of biochemistry at the University of Wisconsin-Madison and the lead investigator and Arthur C. Nielsen Jr. Chair of Metabolism at the Morgridge Institute for Research.

The BJC Investigators Program brings to the School of Medicine scientists whose innovative approaches to addressing important biological questions have the potential to lead to new ways of understanding disease and developing treatments. Eventually, the program will bring 10 highly regarded researchers to the medical school and the St. Louis life sciences ecosystem. Pagliarini is the fifth BJC Investigator named.



Linda J. Richards, PhD, recognized internationally for her expertise in brain development and developmental disorders, has been named head of the Department of Neuroscience and the Edison Professor of Neurobiology. Richards previously served as a professor of neuroscience and the deputy director of research at the Queensland Brain

Institute at The University of Queensland in Brisbane, Australia. Richards investigates how the brain forms during development and how disruptions to normal development lead to brain disorders and brain cancer. Her laboratory investigates the formation of the corpus callosum, the bundle of nerves that connects the two hemispheres of the cerebral cortex. The corpus callosum is affected in many intellectual disability syndromes.

Richards assumed the post in January 2021. She will lead the department as construction continues on an 11-story hub for WashU neuroscience research (see page 2).

A crisis unfolds

Manning Incident



"We all had a common enemy, and that enemy was lethal and creative."

- John Lynch, MD, president of Barnes-Jewish Hospital and professor of medicine

Joining forces

In February 2020, Medical Campus leadership contacted Alex Garza, MD, chief medical officer of SSM Health, suggesting that the three big regional systems — SSM, Mercy, and BJC — get together. "Very quickly after that, we started a dialogue with local elected officials and their public health directors about a collective response to the pandemic," said Clay Dunagan, MD, BJC's senior vice president and chief clinical officer and professor of infectious disease.

he virus had not yet left Wuhan, China, when the School of Medicine, Barnes-Jewish Hospital and BJC HealthCare started bracing for a medical disaster of greater magnitude than any they had ever experienced. Six weeks before COVID-19 reached St. Louis, incident command centers were set up at every BJC hospital, with a joint incident command center for the medical school and Barnes-Jewish Hospital.

or treatment protocols.

Foresight

Two years earlier, foresight had driven the purchase of emergency operations software. "We could send alerts, share information, and customize the platform to gather specific data what critical supplies did we need, how do we get out in front of this?" said Ryan Nicholls, assistant director of emergency management. The incident command center went virtual as soon as it could: "Critical people were making critical decisions, and we could not risk them getting sick," he said.

Vital communication

Information was changing hourly. Communication leaders at WashU Medicine and at Barnes-Jewish and St. Louis Children's hospitals swiftly partnered on messaging to keep vast institutions, multiple sites and experts across many disciplines in sync. At the medical school, Associate Vice Chancellor Joni Westerhouse channeled news to Medical Public Affairs, which disseminated info via a COVID-19 newsletter and website, press releases, social media, podcasts and video.

Employees representing every key operational function reported to the command centers at dawn. They showed the guards their badges, had their temperatures checked, sanitized their hands, wiped down their laptops — then looked up. One long wall was covered with monitors: news bulletins; the hospital's census; global epidemiological charts and maps; regional stats. As information was processed and key decisions made, word shot out to the hospitals, where health-care workers adjusted instantly to changes in safety

The collaboration was unprecedented.



In the early days of the pandemic, protective masks were used for multiple days and stored in paper bags between shifts.

Outlook S

he incident command center conducted briefings each morning and throughout the day and did wrap-ups in the evenings, with some staffers invariably spending the night to keep trying to find N95 respirators or sterile gowns. David H. Perlmutter, MD, executive vice chancellor for medical affairs and dean of the medical school, convened with all department heads and BJC leadership regularly on Zoom, as did many other groups. Infectious diseases clinicians and COVID-19 researchers exchanged information about what was happening at the bedside and about possible diagnostics and treatments being developed in the lab. The Department of Medicine set up a weekly grand rounds series viewed by thousands, offering updates on COVID-19 management and care. And intensivists met for 90 minutes daily with an array of specialists, discussing the intricacies of care for an illness that could attack multiple organ systems.

PPE shortages

"Our typical distributor was out of everything, so we had to open up new supply lines. We do have a relationship with a group in China — we were helping them build an oncology hospital — so they would send us supplies monthly," said Paul Scheel, MD, MBA, associate vice chancellor for clinical affairs and CEO of Washington University Physicians. "Sometimes, the U.S. government would confiscate them at customs and divert them to areas of higher need, so we had no idea what we would have at any given time."



"There was no playbook for this. We had to create an organizational structure. Get the hospital ready for a surge. Figure out how to protect everybody, how to handle telemedicine. Move faculty and staff to remote operations and put classes online. Stop nearly all research and shift the focus to coronavirus." — David H. Perlmutter, MD, dean of the School of Medicine

Massive operational shifts

Labs go quiet.

Going virtual

were virtual."

At the first sign of community spread in mid-March, nonessential employees began working from home and medical school classes went online. Fourth-year students were nearly finished, said Eva Aagaard, MD, senior associate dean and the Carol B. and Jerome T. Loeb Professor of Medical Education. "Their disappointment was missing Match Day — a really strong tradition for us — and graduation, both of which

Stopping research midstream

For safety purposes, the only research projects to continue were those involving rare and irreplaceable samples or months of work that would be undone by stopping. That research was deemed "essential," as was all COVID-19 research. Though shutting down labs was painstaking and laced with disappointment, Jennifer Lodge, PhD, vice chancellor for research, was relieved to see "so much cooperation, so many people wanting to do the right thing." Lodge, also a professor of molecular microbiology, consulted with colleagues at Stanford, Harvard and Columbia, learned best practices from WashU infectious disease experts and set up committees to plan, document and color-code. All the faculty wrote plans for shutting down and reopening labs.

Meeting the challenge

lenovo

• xperts in different disciplines braided and rebraided, forming small work groups to solve problems. Clinical staff were surveyed to see who would be available to pinch hit if, for example, BJH ran out of nurses or the COVID-19 ICUs needed more physicians.

"Some people slept here in the dorms for weeks on end," Scheel said. "It was all hands on deck." A Coping With COVID-19 hotline facilitated by the Department of Psychiatry offered in-the-moment therapy for essential workers, and Human Resources rolled out a wealth of support resources to the entire WashU community as it adjusted to the pandemic. As the COVID-19 census rose, supervised medical residents provided the majority of care for patients who didn't have the virus.

Social distancing does not come naturally in health care, where people work side by side, confer in discreet murmurs in the hallway and support each other. Yet "we had remarkably few workers who became positive," said William Powderly, MD, FRCPI, director of the Institute for Public Health, "and the majority of those who did acquired the infection in the community."

Advising the region

With CDC guidance limited and changing, infectious disease docs worked even harder to inform the public — doing a raft of media interviews and helping St. Louis strategize closing and reopening. The infectious diseases division provided the state of Missouri with data analysis, modeling and research. Between the Institute of Informatics at the School of Medicine and the health-care informatics at BJC, physicians and civic leaders were able to see where admissions were occurring, to understand who was at higher risk for hospital admission or critical care and to predict surges. That level of analysis was not available in many parts of the country. "Our position in this community and the expertise we bring to the table mean that the work we do reverberates far beyond our walls," Dean David Perlmutter said.

Testing breakthrough

From the outset of the pandemic, clinicians and researchers began looking for an alternative to nasal testing, which requires reagents and special swabs that were in short supply nationally. "One of Dr. Perlmutter's early charges was to develop novel testing," said Paul Scheel, CEO of Washington University Physicians. The McDonnell Genome Institute promptly developed a rapid, accurate saliva test. The test was used to physically reopen the Danforth Campus in September, and Missouri's governor worked to make it available across the state.

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"We had to change our questions — not 'Do you feel sick?' but 'Do you have a fever?' — because health-care workers are soldiers."

- Jennie H. Kwon, DO, MSCI, associate hospital epidemiologist, on tracing exposures

Infection control

While the COVID-19 care providers fought the virus, their colleagues kept it from spreading through the hospital. A team co-led by epidemiologist Jennie Kwon and infectious diseases specialist Hilary M. Babcock, MD, MPH, built a system to trace contacts among patients and employees and monitor and assess changes. A COVID-19 call center also opened to evaluate symptoms of WashU and BJC employees and checkpoints were established to screen everyone entering the campus. To check temperatures, Scheel realized the perfect solution would be the thermal cameras used to screen people at airports.



"The pandemic has pushed the genius of human innovation to move more quickly to do things that sometimes we prohibit by regulation and hesitancy."

- Brent Ruoff, MD, associate professor of emergency medicine

Changes in health care

"Telehealth for sure is here to stay," said Victoria Fraser, head of medicine, "particularly for vulnerable patients who live at a great distance or have trouble with mobility." The necessity of infectious disease specialists is newly realized, said public health institute director Bill Powderly, adding that "over half of U.S. hospitals don't have an ID specialist."

ather than be paralyzed by this crisis, "we used it," said Victoria Fraser, MD, the Adolphus Busch Professor of Medicine and head of that department. "People had been slowly working on online education and telehealth for years, and because of COVID-19, we started them up in a couple weeks." It also took only two weeks to stand up the new respiratory clinic, an endeavor so complicated it would normally involve years of planning. "In our normal way of working together, we work until we get it exactly right," BJH President John Lynch observed. "Perfectionism runs rampant on both sides of Euclid Avenue. It makes us great institutions, but it doesn't make us nimble.

"There is a sense now that together, BJH, BJC and WashU can solve problems of a magnitude we had never actually even contemplated," he said. "That we can take on challenges so big they weren't even imaginable."



Readiness for tomorrow

"The way we used the Joint Incident Command Center will help us solve future problems," Lynch said. "It will be incredibly helpful to have the centralized ability to move staff where they are needed and balance our patient volumes across our campus and throughout our healthcare system. It was amazing to watch the School of Medicine point its considerable resources at COVID-19 and develop its own COVID-19 test within weeks, then bring on an instrument that could do 1,000 tests a day!" The medical center now has stockpiles of emergency supplies that are expected to last many months. "We have learned how to manage thru COVID-19," Scheel said.

Reported by Jeannette Cooperman

Significant firsts

BY KRISTINA SAUERWEIN

First-year medical students pose for a socially distanced class portrait. The 105 physicians-to-be received their white coats, considered the first symbolic step into the medical profession, and started their medical journey with family and friends watching remotely.

II

6 Washington University School of Medicine

Entering class of 2020 undertakes new Gateway Curriculum in pandemic

chool of Medicine faculty knew that major shifts in the educational landscape would occur in 2020 with the rollout of a new curriculum. Three years in the making, the Gateway Curriculum would be the school's largest and most comprehensive reform in decades.

What they didn't expect was an earthquake in educational disruption — and months of aftershocks.

In March 2020, as dozens of faculty fine-tuned the Gateway Curriculum, readying it for a fall launch, the SARS-CoV-2 virus aggravated its spread in the U.S., jolting much of the nation into unprecedented lockdowns.

Halfway through spring semester, COVID-19 safety concerns emptied the medical school. Nonessential employees scrambled to pack office and lab necessities for indefinite telecommuting. Lectures and labs, classes and clinical rotations came to a halt. Instead of spring-break downtime, many students moved back home, not knowing when they'd return; others quarantined in nearby apartments.

The urgency of the crisis left little time to tie loose ends or say goodbye to mentors and friends. Students wondered if they'd be able to finish their courses required for ascending to the next level of training. "COVID-19 uprooted everything we were striving toward," said Eva Aagaard, MD, the senior associate dean for education, who has spearheaded curriculum revision. "But we quickly realized it would not stop us from moving forward.

"Fortunately, we discovered our years of hard work designing the new curriculum and making the necessary investments in technology uniquely prepared us to transition from in-person to remote learning," said Aagaard, also the Carol B. and Jerome T. Loeb Professor of Medical Education. "During the curriculum-building process, our collective mindset had become more accustomed to embracing change and innovation while pushing creative boundaries. These qualities made it easier to weather the abrupt move to distance learning and, more broadly, uncertainties surrounding COVID-19."

The new curriculum prepared the medical school not only to survive but thrive during the rapidly changing, ongoing emergency crisis.

"Faculty felt the shock and stress. However, we knew we had no time to waste in transitioning academic instruction to an electronic platform," said Thomas M. De Fer, MD, a professor of medicine and associate dean of medical student education. "Because of the planning and investments that had gone into revising the curriculum, we were able to do this efficiently and effectively."



Targeted technology

Already in place was much of the medical school's upgraded, top-ofthe-line technology supporting videobased education and online interaction between faculty and students. Over a year earlier, the Instructional Design Studio opened in a 700-square-foot space in Bernard Becker Medical Library. It includes both a formal soundproof video-recording studio with green-screen technology and a smaller do-it-yourself studio. The space allows faculty to record lectures with supplemental and interactive features that the medical school can archive in a digital library and students can access at any time.

"We have worked closely with faculty to examine how we will deliver parts of the new curriculum through video resources, and to create and produce dynamic, high-quality, clinically relevant video resources to enhance student engagement with course materials and promote meaningful, durable learning," said Carolyn Dufault, PhD, assistant dean for educational technology and innovation in the Office of Medical Student Education.

Technology also enabled third-year clerkships to safely resume over summer. Students transported virtually to the school's Wood Simulation Center, where rooms resemble clinical settings and mannequins serve as patients. Computer screens offered multiple vantage points of the patient and vital signs. Technician Brittany Novak operated the simulator and acted as the patient's voice, while Julie Woodhouse, registered nurse and director of the medical school's immersive learning centers, served as the bedside nurse, following the students' patient-care directives.

"The clinical experience encouraged students to determine diagnosis and treat patients in acute scenarios in a safe setting and without faculty or residents instructing them on how to manage the situation," Woodhouse said. "The experiences may have felt artificial or awkward, but I asked the students to think of it like telehealth or an electronic intensive care unit, where the physician is in a separate location from the patient and bedside staff. The pandemic has put a spotlight on telehealth. It's likely to continue to play an increased role in patient care."

Despite havoc wreaked by a global pandemic, the new curriculum launched in September with the 105 aspiring physicians comprising the entering class of 2020.

Larissa Lushniak of Rockville, Md., felt apprehensive beginning her first year of medical school with a new curriculum and during a pandemic. "But the use of innovative technologies and engaging virtual lectures have made learning extremely successful," she said. "I've also found that learning clinical skills virtually has placed a greater emphasis on the importance of effective communication skills and forming strong physician-patient relationships. This is critical because, as physicians, we may see a patient in an exam room or virtually via telemedicine."

Anticipated blips and bumps notwithstanding, Aagaard said the first few months of the curriculum rollout proved smooth. "The pandemic tested the new curriculum's foundation," she said. "Throughout, its pillars, its core values, demonstrated stability and strength."

As part of their training,

students direct treatment

Saigh Pediatric Simulation

Center. Computer screens

offer multiple viewpoints

of the patient.

decisions through the school's

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In the wake of George Floyd's death in police custody, students organized a White Coats for Black Lives demonstration this summer on campus. Thousands of faculty, students and staff raised their voices, insisting racism is a pandemic, too.

Students mobilize in public health crisis

After the March 11 announcement by Chancellor Andrew D. Martin restricting in-person academic instruction, many medical students wondered what to do. They had taken an oath committing to patient care and human health. As trainees, they lacked certification to help on the pandemic's front lines. But many students found it unthinkable to remain on the sidelines as a worldwide health crisis escalated.

Two days after the announcement, three medical students issued a call to action via email and social media. Within 24 hours, more than 100 students had signed up to volunteer. Two weeks later, the number doubled.

Among the volunteer activities, students delivered meals to at-risk quarantined people and COVID-19 patients, provided child care for

"As a student, it was empowering to be in useful roles during a time of great uncertainty." — Bruin Pollard

health-care workers, and created thousands of face shields and masks. They also assisted with contact tracing at area health departments and offered educational outreach to St. Louis' African American and Latino residents, who are most at risk to COVID-19's adverse effects. Overall, more than 12,000 student volunteer hours were recorded.

"As a student, it was empowering to be in useful roles during a time of great uncertainty," said Bruin Pollard, then a first-year medical student who initiated the call to action with Christopher Chermside-Scabbo and Cyrus Ghaznavi, then a fifth-year MD-PhD candidate and a second-year medical student, respectively. "One of the qualities of Washington University's medical school that students appreciate is encouragement to engage with the community and to help those who are the most vulnerable."

Addressing social and economic barriers to good health is the hallmark of the new curriculum, a continuous thread woven throughout students' courses, lectures, research and clinical experiences.

From day one, students learn that patient care requires focusing on the whole person rather than a single illness or disease. This is because characteristics such as race, gender,

sexual orientation, income and neighborhood can influence health outcomes — a phenomenon medical and social scientists refer to as social and structural determinants of health.

"Since the beginning, we've integrated the building blocks of basic science, ethics, community engagement, health-care systems, professional and public health, which has thoroughly enriched my understanding of holistic medical education" said Carly Duncan, a first-year student from Modesto, Calif. "The curriculum's emphasis on teaching students to understand patient narratives, evaluate the impact of social and structural determinants of health, and practice trauma-informed care has opened my eyes on the importance of the physician-patient relationship and of examining medicine through compassionate lenses."

An overarching curriculum goal is to improve the health of the St. Louis region and beyond by building upon existing community and university partnerships as well as creating new ones. Medical students accomplished this in March, shortly after area stay-at-home orders were issued to control the spread of COVID-19.

Then a first-year student, Austin Ibele worried whether coronavirus information existed in Spanish to alert the area's Latino population about the lockdown. He felt dismayed when he found nothing on local government and health department websites.

After hours of scrolling social media feeds, Ibele eventually found a Spanish-language Facebook page named "STLJuntos," which translates to "St. Louis Together." The newly created page had few followers but offered updates on local stay-at-home mandates and links to the Centers for Disease Control and Prevention's Spanish-language coronavirus page.

In less than a day, Ibele and other medical students had partnered with the two women who had created STLJuntos. All shared the same urgency to expand COVID-19-related outreach and educate the region's Spanish-speaking communities.

Throughout the U.S., underrepresented minorities living in low-income communities with limited access to health care represent a disproportionate number of COVID-19 cases and deaths. Social and economic conditions predispose them to higher rates of chronic obstructive pulmonary disease (COPD), diabetes, heart disease and other illnesses that aid the virus in weakening the body's organs. In addition, social inequities in income, housing and jobs result in challenges with social distancing and quarantining, as well as access to care.

"Health disparities exist during normal times, and these inequities are compounded when something new comes along like coronavirus," Ibele recalled. "That's why it is extremely important to make sure all members of the public are educated." Student volunteerism to combat COVID-19 inspires Ian Marigi, a first-year from Brooklyn Park, Minn. — as does the Gateway Curriculum's emphasis on eliminating health and racial inequities. Integrating social justice with science and medicine is one of the primary reasons why he wanted to attend Washington University. "As an East African immigrant, I understand some of the obstacles that underrepresented minorities face in health care," Marigi said. "COVID-19 has inflamed many of the health disparities that come with different personal identities. I'm excited to be at a medical school that acknowledges this reality and is active in addressing it."

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To assist with the outbreak, medical students Sirui Ma (left) and Meg Landon perform contact tracing at the St. Louis County Department of Public Health.

Medical students Eric Balta (left) and Garrett Wahl manufacture reusable face shields to be placed over N95 or surgical masks. Students responded to a call to action from Victoria J. Fraser, MD, the Adolphus **Busch Professor of Medicine** and head of the Department of Medicine. At one point early in the pandemic, students made 1,600 masks in just three days, using plastic sheeting, cushion foam, elastic fabric and weatherproofing seal.

'It's why we got into medicine'

Fierce sense of mission drives front-line workers

BY JEANNETTE COOPERMAN

In February 2020, Hilary Babcock, MD, MPH, professor of medicine and a specialist in infectious diseases, gave a talk at a conference in Yokohama, Japan. From her hotel window, she could see the gleaming white cruise ship, the Diamond Princess, docked. At the conference breaks, local doctors talked to her about how they planned to care for COVID-19 patients from the ship.

She helped them strategize, but she was cold with dread. This was a brand-new virus, and Babcock, medical director for infection prevention and occupational health at BJC HealthCare, knew it would spread like wildfire. No one was immune. No one was protected.

A week after she flew home, Washington University sent word to all overseas students and faculty to return to the United States. Babcock focused on ways to keep health-care workers safe while they cared for patients. "That rapidly became much more complicated," she said, because the personal protective equipment (PPE) they needed was in short supply. "For everything we looked at — even IV tubing, saline, commonly used drugs — there were shortages."

The care team, including (left to right) nurse Kyle Breitenstein, respiratory therapist Melissa Delavara and nurse Hannah Peterson, prepare to move a patient to the prone position.

fter talking with friends in Italy, where the hospitals were aflame with the virus, Tiffany Osborn, MD, MPH, professor of surgery and of emergency medicine, had bought herself some extra PPE online. Better to have and not need, she thought. Then the virus exploded in New York.

Daniel Theodoro, MD, MSCI, assistant professor of emergency medicine, had trained there, and several of his former colleagues fell ill, one ending up on a ventilator. Theodoro was terrified; he has young children at home. "The only other time I was this scared was while I was on shift when the Twin Towers came down," he said. "I was privy to the radio transmissions, and there were all these rumors in the fog of war That is the only thing equivalent to the panic that was coursing through our veins daily."

In those early days, "it felt that if you were to walk through a plume of COVID cough you'd end up dying and contaminating your entire family," Theodoro continued. He kept seeing photos of Chinese physicians covered head to toe in plastic - and here he was, making an N95 mask last for days when normally, he would have discarded it after one interaction with a patient.

Even tests were in short supply. "Ideally you would want to be able to test anyone you think might have it," Babcock said, "but at the beginning, across the whole country, the testing was so limited. That made it very hard to get our arms around how many cases there really were. And we didn't yet know how much of an issue asymptomatic transmission was going to be."





Cristina Vazquez Guillamet, MD, assistant professor of infectious diseases and pulmonary and critical care medicine, and Rodrigo Vazquez Guillamet, MD, associate professor of medicine in the pulmonary and critical care division, felt an impossible pressure: "We cannot be on the sidelines of this. It is our duty. But we cannot risk the lives of our little boys" — or of Cristina's parents, who live with them and help with child care.

They decided to stay at the Knight Executive Education & Conference Center on the Danforth Campus, which was swiftly converted into a hotel for health workers. This way they could focus, starting work before 7 a.m. and ending after 7 p.m. Then they'd strip off their PPE and race back to the hotel to shower and Facetime their little boys — this was the first time they had ever been parted — before the boys' bedtime.

Cristina had always wondered about the bond between soldiers; now, joking with the nurses as they checked each other's PPE for a tight fit, she felt what she imagines is the same camaraderie. But she also felt a consuming fear. "Women don't seem to get as sick," she told Rodrigo. "I think I should take the ICU shift for both of us."

"Are you out of your mind?" he shot back. There was no guarantee of safety anywhere. "You're staring your mortality in the face," said Brent Ruoff, MD, associate professor of emergency medicine. "Especially those of us over 60 - we can kind of stuff that down internally, but it did create stress." His older brother has disabilities, and Ruoff takes care of him. He called their sister and let her know that if worst came to worst, she might have to take over.

Staying safe

As the days went by, though, it became clear that the PPE, tightly rationed as it was, worked. "At first I would gel (sanitize) about 50 times just taking my shirt on and off," Theodoro admitted, laughing. "Now I'm like, unless someone came in here and licked the counters, I'm probably OK."

The emergency department, after all, was the proving ground. These were the docs doing triage, Precautions were stringent throughout the

testing, often intubating before sending the patient upstairs. And in all this time, said Rob Poirier, MD, assistant professor of emergency medicine and clinical chief of the department, there has not been a single case of transmission between or among patients and staff. hospital, and they saved lives, but they came at a cost. "The distancing really affects me," said Ken Remy, MD, MHSc, MSCI. One of the nation's few adult and pediatric intensivists, he spent significant time on COVID-19 international response teams advising various international ICUs. Early on, he spent practically "more time than anybody" in the COVID-19 ICUs across the BJC network because of his adult and pediatric expertise — despite a preexisting condition, a worried family, and multiple showers a day. But what he could not bear was the isolation. Nurses would write "You are loved" on the glass so a patient could see it the minute they woke, but the only way they could see loved ones was on an iPad the hospital supplied (and med students taught families how to use).

Health-care workers write

a message of support on a

wall facing a patient's room

in a COVID-19 ICU.

Rodrigo Vazquez Guillamet, MD, and Cristina Vazquez Guillamet, MD, play with their sons in Forest Park. While taking shifts in the ICU this past spring, the doctors made the difficult decision to stav in the Knight Executive **Education & Conference** Center on the Danforth Campus to protect their sons and Cristina's parents who help with child care from COVID-19 exposure.

The no-visitors policy eased to one visitor in late June. By then, Rodrigo Vazquez Guillamet had listened to a 20-year-old sobbing because her mother was dying, and she could not even say goodbye in person. "Look," he said to senior administration, "we have to keep our humanity through this."

So they changed the rule. "And we were so grateful," Cristina said.

She also was deeply gratified by all the collaboration. Physicians from unrelated specialties, pulled from their own research or clinics for safety's sake, pitched in — dermatologists staffing the COVID-19 call line, cardiologists and pulmonologists volunteering to work in the COVID-19 ICU, nephrology researchers making DIY hand sanitizer for the dialysis centers, med students designing face shields.

"The one thing nobody could predict when it was really at the peak, was how relentless it would be. How tired you would be. It just. Didn't. Stop."

— William Powderly, MD

New information came daily, and what was useful had to be sifted from speculation, anecdote and politicized federal guidance. "The texts and emails began before 6 a.m.," said Michael Lin, MD, associate professor of medicine and interim chief of hospital medicine. "Then it was all about trying to respond and anticipate staffing needs, clinical needs, PPE, cleaning supplies, work space distancing, provider wellness — through close to midnight. Things were being done on the fly there were changes even from morning to night in the recommendations and the staffing. It really was building a plane while you are flying it." Among those in the control tower was William Powderly, MD, FRCPI, the Dr. J. William Campbell Professor of Medicine, Larry Shapiro Director of the Institute for Public Health, director of the Institute for Clinical and Translational Sciences, and co-director of the Division of Infectious Diseases. He had never had to multitask with an urgency this intense. Still, every day he pried himself away from the administrative work, donned a mask, and went to talk with fellows and trainees who were seeing patients. "It reminded me of why I was doing this," he said, "and it grounded me."

One of the many bits of information he captured was how often patients lost their senses of taste and smell. "That wasn't written anywhere yet; it wasn't in the CDC protocols. But we put it into ours, because it made biological sense, and we were hearing it from a significant number of patients, as many as 10%, and for quite a few, it was their only symptom."

The daily trick, clinically, was to balance caution and resolve, staying patient but learning constantly. "The one thing nobody could predict," Powderly said, "when it was really at the peak, was how relentless it would be. How tired you would be. It just. Didn't. Stop."

Exhaustion and exhilaration

"As stressful and scary as the initial days were, it was an exciting time, because everyone was sharing information," said Colleen McEvoy, MD, assistant professor of medicine. Protocols, clinical observations, research findings, and ideas flew between institutions, and the experts at WashU offered guidance to public health departments and other hospital systems. "The whole focus was the patient and the disease," McEvoy said, "and that's why we got into medicine. That's why we could work 14- and 15-hour days."

They worked those days for months, though, many without a weekend off, and administrators heard zero complaints. "There was very little evidence of ego," Powderly said. "People just knuckled down to solve the problems."

McEvoy and Osborn became co-directors of the COVID-19 Critical Care Task Force, anticipating scenarios and creating guidelines. Which treatments might heighten contagion? High-flow oxygen could keep the lungs open, but it would



send air into the room, but new data showed that when the person wore a mask, that extra exposure was virtually canceled out. They talked, at all hours of the night, with colleagues around the world and on the coasts. Those anesthesiologists who were no longer in the OR because elective procedures had been canceled? Put them on a procedures team, docs in Seattle suggested, so they can intubate and put in central lines while the pulmonologists deal with ventilators. The common wisdom at the outset was to rush to intubate, but that turned out to be unnecessarily aggressive. "Normally, I'll intubate one or two people every month," said Theodoro, "and colleagues in New York were intubating one or two an hour."

Physicians gathered up practical bits of guidance wherever they could. Proning helped, said Remy, because when patients rolled over to lie on their stomachs, the bottom of the lungs could fully expand. Clotting was a special danger; blood flow was key, and the linings of arterial vessels could inflame. Lungs of COVID-19 patients were not heavy and wet, as they are with influenza, but supple — that was odd — and patients with extremely low oxygen saturation sat there playing on their phones, not even short of breath. Some patients only had neurological symptoms, like dementia; could that be what had happened to

Charge nurse Caroline Becker cares for a COVID-19-positive patient.



the New York physician whose suicide haunted everyone? Or was she just worn down by the trauma of all she had seen?

Societal complications

St. Louis waited, nerves on edge. But thanks to weeks of meticulous planning, the ED and six COVID ICUs managed incredibly well, even when cases were at all-time highs. And by the end of April, the first surge began to come down.

Over time, the COVID-19 teams developed a good sense of how to take care of these patients. They also knew how to stay safe, so personal fears were easing — but social tensions were ratcheting up, the heightened anxiety and despair creating a bleak landscape.

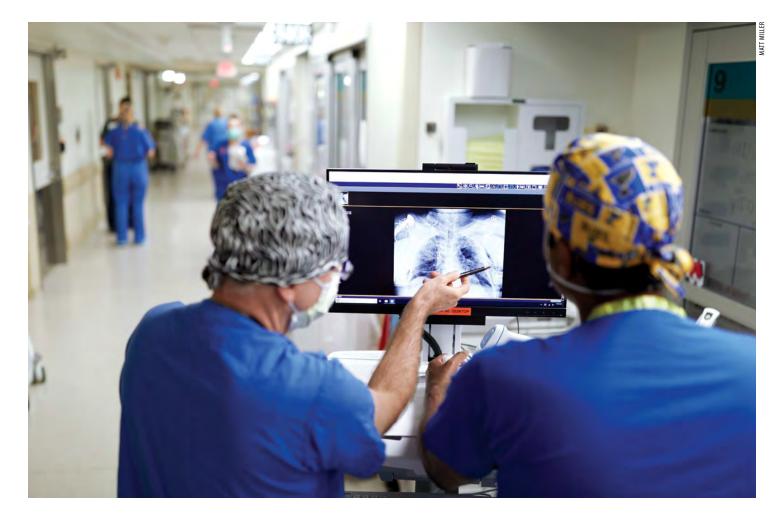
"Since COVID-19 started, our community violence rate has dramatically gone up," said Poirier of the emergency department. "The number of people shot has gone up 30% to 50%, and there are more suicides and suicide attempts and more drug-related issues, sometimes in people with two, three, even four different drugs in their system at once." People without homes were insisting they could quarantine under a bridge and tell people to stay away.

"It kind of feels like the four horsemen are riding into town," Ruoff remarked to a colleague.

Nationwide, doctors began expressing concerns that the CDC, which always has been a steadying voice of authority, seemed to be delaying or changing its guidance due to political pressures. "You had to sift through recommendations that were coming out of Atlanta and D.C. and try to understand what the different pressures were," Powderly said. "We're fortunate in that quite a number of the infectious disease faculty have held national leadership positions, so we know quite a number of people at the NIH and CDC. That allows us to have a better understanding of the dynamics."

Still, there was no looking things up. The textbooks on COVID-19 had not yet been written. The only way to move ahead was to let the virus itself teach them.

Another intersection of society and medicine was the disproportionate number of patients who were African American. It was surreal enough to see an entire ICU filled with patients who had only one kind of sickness, Cristina Vazquez Guillamet



said, but then to see that the majority of them were Black, more vulnerable for a long list of reasons laced with mistrust and inequity? "We have to do something about this," she told Rodrigo. "At the end of this, we have to be better humans."

That was the impulse that brought WashU docs outside, the sun reflecting off hundreds of white coats as they lined Kingshighway Boulevard, protesting for racial justice after a police officer in Minneapolis knelt on George Floyd for more than eight minutes while he gasped, "I can't breathe." Asked by a USA Today reporter if protesting was a public health risk, Babcock pointed out that systemic racism is also a public health risk. Will Ross, MD, MPH, professor of medicine and associate dean for diversity, co-authored a study that found African Americans to be 16% of the region's population — and 34% of its confirmed COVID-19 cases.

A new and lethal pandemic, grueling hours, wrenching isolation, social tension — what has kept WashU's docs going all these months? A fierce sense of mission, of responsibility. This was what they had trained to do, what they could do when others couldn't. Also, notes Cristina Vazquez Guillamet, "there was the intellectual curiosity. We wanted to understand." What was hard was risking your life and your family's, witnessing so much suffering and sacrifice, then hearing people insist that the virus was a political exaggeration, the precautions a conspiracy. "People find out you're a doctor, and they want you to tell them, 'Yeah, it's nothing," Theodoro said. "When you say, 'No, I've seen it,' the incredulity — it can't register."

At the bedside, though, all denials and arguments and alternate realities vanish, and only care remains. "When you look at a patient, you don't see their political views," said McEvoy. "It doesn't matter if they thought COVID was real or not." \Box

Physician assistant David Schlictman, PhD, (left) and pulmonologist Praveen Chenna, MD, discuss a chest X-ray.

COVID-19

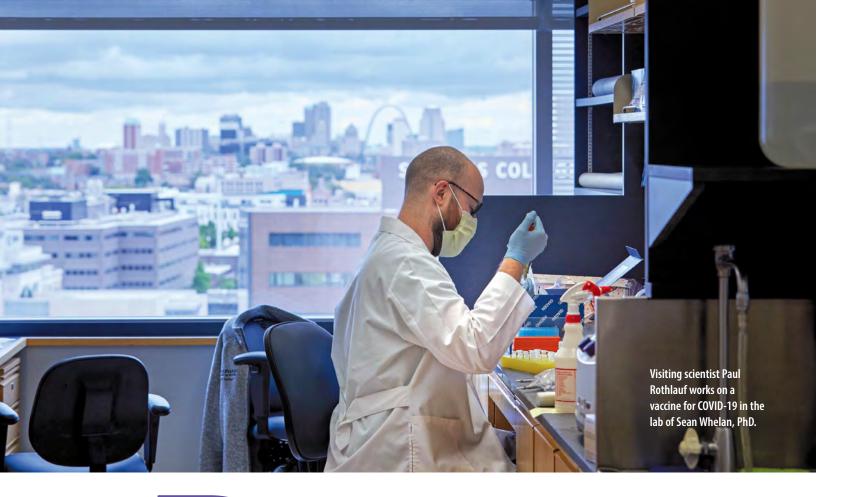
Medical school labs pivot to fight a common enemy

BY TAMARA BHANDARI

In early January 2020, Sean Whelan, PhD, the new head of molecular microbiology, met with Michael S. Diamond, MD, PhD, the Herbert S. Gasser Professor of Medicine. The two virologists, both active in the world of emerging infectious diseases, discussed reports of a mysterious new coronavirus that had sickened a few dozen people in the central Chinese city of Wuhan, and considered whether it was significant enough to study. No deaths had been reported.

Over the coming months, the new coronavirus would spread around the world, infecting tens of millions of people, killing more than 2 million and transforming the day-to-day lives of just about everyone. At the School of Medicine, scientists and physicians would launch themselves into the frantic worldwide effort to end the pandemic.

Postdoctoral researchers Brett Case, PhD, (foreground) and Adam Bailey, MD, PhD, work on the novel coronavirus in a biosafety level-3 lab in the McDonnell Pediatric Research Building. Early in the pandemic, Michael Diamond, MD, PhD, received the SARS-CoV-2 strain from the CDC.



esearch labs retooled to investigate how the virus causes disease and to develop drugs, vaccines and diagnostics to curb its destructive effects. Informatics scientists developed models to find hot spots of infection, predict the spread of the contagion and guide public health interventions. Physicians hastily set up clinical trials to evaluate whether therapies and preventives designed for other conditions could be repurposed for COVID-19.

But all that lay in the future. In the first week of 2020, neither the virus nor the disease it caused had even been named. Whelan and Diamond still thought it possible that the outbreak would be contained, as nearly all outbreaks are, and relegated to a footnote in the history of public health.

Building the research infrastructure

By February, the novel coronavirus had spread to every province in China and a dozen countries, including the U.S. The World Health Organization had declared it a Public Health Emergency of

International Concern. What was once a curiosity was shaping up to be a global pandemic on a scale not seen in over a century.

Curbing the pandemic would require information — and quickly: How is the virus getting into the body and around its defenses? Who is getting sick, and why are some people recovering while others are on ventilators? Where are the virus's weak spots, and how could they be targeted?

Whelan teamed up with William G. Powderly, MD, director of the university's Institute for Clinical and Translational Sciences (ICTS), and Jeffrey Milbrandt, PhD, the James S. McDonnell Professor of Genetics and executive director of the McDonnell Genome Institute, to create a COVID-19 research task force.

Whelan, also the Marvin A. Brennecke Distinguished Professor of Molecular Microbiology, took the lead on basic virology research. He coordinated Monday morning research meetings and set about establishing a high-level containment laboratory to safely study the novel coronavirus, officially named SARS-CoV-2 in February.

Because the virus is spread through the air and potentially deadly, working with it requires biosafety level-3 containment. Scientists handling the virus must wear biohazard suits with pressurized respirators, and work inside labs

with multiple containment levels and specialized ventilation systems.

As an incoming department head, Whelan had been assigned ample lab space, including a room suitable for use as a biosafety level-3 laboratory. But in February, the room sat empty as Whelan's equipment and supplies were still being shipped from his old lab in Boston. Luckily, a brand-new -80° freezer had been left in a nearby hallway by Christina L. Stallings, PhD, an associate professor of molecular microbiology, while she reorganized her space. Stallings volunteered the freezer — Whelan replaced it later — and, with Diamond's help, outfitted the room with necessary equipment so it could be certified as a biosafety level-3 lab.

While Whelan prepared a place to work, Diamond started emailing contacts at the Centers for Disease Control and Prevention (CDC) to request access to the new coronavirus. Diamond was well known at the CDC, having conducted seminal early research during the Zika epidemic, such as creating the first pregnant mouse model and identifying protective antibodies. On Feb. 5, the CDC overnighted him a small frozen vial containing virus obtained from the first person diagnosed with COVID-19 in the U.S.

Powderly, also the J. William Campbell Professor of Medicine and the Larry J. Shapiro Director of the Institute for Public Health, coordinated COVID-19 clinical research through the ICTS. Jane A. O'Halloran, MD, PhD, an assistant professor of infectious diseases, and Philip Mudd, MD, PhD, an assistant professor of emergency medicine, already had begun creating a central biorepository of COVID-19 specimens through the School of Medicine's Emergency Care Research Core and the Infectious Diseases Clinical Research Unit. They were collecting blood, urine and stool samples as well as nasal swabs from people diagnosed with COVID-19.

"There was a lot of concern that so many researchers would be looking for samples that it would get overwhelming for participants," O'Halloran said. "We decided we needed to streamline the process so each patient would only be approached once and the whole community would have access to specimens."

Powderly tapped Christina A. Gurnett, MD, PhD, a professor of neurology and the associate director of ICTS, to oversee access to the biobank. With colleagues, Gurnett reviewed nearly 200 applications from faculty in 18 medical school departments, as well as the McKelvey School of Engineering, and Arts and & Sciences.

Researchers proposing similar projects were put in contact with each other to combine efforts. "The goal wasn't to restrict access; any request we got we tried to honor," Gurnett said. "But these samples are a precious commodity, and we wanted to make sure we got the samples to the people who could make the best use of them right away." By the end of October, 15,336 samples from COVID-19 patients had been distributed to more than 23 investigative teams. O'Halloran and Mudd signed up their 500th patient Sept. 29, completing enrollment in one of the most comprehensive COVID-19 specimen collection programs in the country. They continue to collect samples for studies of the long-term effects of SARS-CoV-2 infection.

Stemming the tide

As COVID-19 continued to spread throughout the U.S. that spring, it became clear that national- and state-level models couldn't provide the detailed information about local transmission that officials needed to make public health decisions. "A lot of local public health agencies started developing models on their own to get locally relevant projections, and that is a heavy lift," said Elvin H. Geng, MD, a professor of medicine who studies the effect of public health interventions on HIV infection rates. "We thought it would be helpful to develop a modeling platform that is sophisticated enough to give realistic – and publicly available — results, but simple enough that it can be accessed by an informed public health user."

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Principal investigator Jane O'Halloran, MD, PhD, talks with volunteers who are participating in a study to evaluate large-scale COVID-19 saliva testing.



Geng and colleagues at the University of California, Berkeley, created a platform and made it publicly available on GitHub. The state of Missouri is using the platform to improve regional awareness, forecast epidemics in localities across the state and inform planning efforts. A group of hospitals in St. Louis is using the platform to project the need for hospital beds in the region.

The search for treatments

As public health officials worked to stem the tide of cases, Rachel M. Presti, MD, PhD, an associate professor of medicine and director of the university's Infectious Diseases Clinical Research Unit, spent the spring trying to get COVID-19 patients access to experimental therapies. But deciding which trials to sign on to was no easy task.

"We reviewed lots of protocols from companies and from faculty," Presti said. "Everyone had an idea of how to intervene. There were endless discussions about the best ways to treat people."

The clinical research unit launched a homegrown clinical trial in the spring to test chloroquine and hydroxychloroquine as COVID-19 treatments, and was involved in some of the earliest work with blood plasma from COVID-19 survivors. They also signed on to national and international drug and vaccine clinical trials, including trials of the Janssen vaccine, a monoclonal antibody as a preventive and a different monoclonal antibody as a therapy for COVID-19.

Benjamin Swan, (right) research nurse coordinator, administers either the MMR vaccine or a placebo to a health-care worker, as part of a global clinical trial enrolling up to 30,000 participants.

Then, an invitation arrived to join Accelerating COVID-19 Therapeutic Interventions and Vaccines (ACTIV), a public-private partnership coordinated by the National Institutes of Health (NIH) to speed development of the most promising treatments and vaccines. These trials were designed to test multiple drugs at once against a single comparison group, minimizing the number of people who would receive a placebo. In addition, the trials could adapt to new data and easily add promising new drugs to the protocol.

Powderly is the head of one of the international ACTIV trials for hospitalized patients. That trial is investigating the potential of three antiinflammatory drugs to normalize the immune response, shorten hospital stays and reduce the need for patients to be placed on ventilators to help with breathing. The goal is to enroll 2,200 patients with moderate to severe COVID-19 across the U.S. and Latin America.

In another prevention effort, a team led by Eric J. Lenze, MD, the Wallace and Lucille Renard Professor of Psychiatry, and Angela M. Reiersen, MD, associate professor of psychiatry, investigated the drug fluvoxamine for people with mild to moderate COVID-19. Fluvoxamine is used to treat obsessive-compulsive disorder, but it also regulates inflammation, which led the investigators to believe the drug could help in COVID-19. In November, Lenze and colleagues published the results of the trial in JAMA, showing that people who received the drug were less likely to require supplemental oxygen or hospitalization. A larger confirmatory trial is starting and will recruit nationwide.

Meanwhile, Michael S. Avidan, MBBCh, the Dr. Seymour and Rose T. Brown Professor and head of the Department of Anesthesiology, was searching for ways to protect the people on the front lines from infection or at least from severe disease. With colleagues at University College London and the University of the Witwatersrand in Johannesburg, Avidan established the CROWN Coronavirus Prevention (CORONATION) trial to test the measles, mumps and rubella (MMR) vaccine. Normally given in childhood, the MMR vaccine seems to induce a generalized immune boost that protects the recipient against a wide variety of infectious diseases for several months. The trial is enrolling up to 30,000 health-care workers in Africa, Europe and North America.



Unraveling a virus

While physicians sifted through known drugs and vaccines in search of something that could prevent or treat the growing number of cases, scientists started dissecting the virus's deadly nature to find new avenues for preventives or therapies.

First, they needed an animal model so they could study the immune response, map the disease course and test out potential drugs and vaccines in a living body. But there was a problem: Mice, the workhorses of biomedical research, are naturally resistant to SARS-CoV-2. In 2007, Carmen M. Halabi, MD, PhD, then a medical scientist training program student at the University of Iowa and now an assistant professor of pediatrics at Washington University, created a strain of genetically modified mice susceptible to infection with the SARS virus, a close cousin of SARS-CoV-2. When the COVID-19 pandemic arose, such mice became highly sought after because they were expected to be susceptible to the new coronavirus as well. But there were not nearly enough to go around.

So Diamond opted to create his own mouse model. He used a mild respiratory viral vector carrying a human gene to make mice temporarily



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Siteman Core Lab Services at the BJC Institute of Health processes COVID-19 blood, saliva and urine samples for research six days a week.





susceptible to SARS-CoV-2 infection. Then, he infected mice with SARS-CoV-2 virus grown from the original sample shipped by the CDC. A description of this model was published in June, providing a path to studying COVID-19 for researchers who couldn't get their hands on a genetically modified mouse.

At the same time, Diamond and Whelan started work on a vaccine using a design platform that had been successfully employed to create a vaccine for Ebola. They created a hybrid virus by swapping a gene from a mild virus with one from SARS-CoV-2, and showed that it protected mice against pneumonia by preventing infectious virus from gaining a foothold in their lungs. It is now being tested in nonhuman primates.

The hybrid virus was created as a vaccine candidate, but it could double as a research tool for scientists who lack access to a biosafety level-3 facility. It infects cells like the authentic SARS-CoV-2, but since it's based on a harmless virus, it can be handled under ordinary laboratory safety conditions. After Diamond and Whelan published a report on their hybrid virus, requests for it poured in from around the world.

"I've never had this many requests for a scientific material in such a short period of time," Whelan said. "We've distributed the virus to researchers in Argentina, Brazil, Mexico, Canada, the UK, Germany and, of course, all over the U.S."

Diamond also worked with David T. Curiel, MD, PhD, the Distinguished Professor of Radiation Oncology, to create a vaccine that could be delivered through the nose, typically the initial site of infection. In mouse studies, Curiel and Diamond found that the nasal delivery route created a strong immune response throughout the body, but it was particularly effective in the nose and respiratory tract, preventing the infection from taking hold in the body. Later studies — in hamsters with Jacco Boon, PhD, an associate professor of medicine,

"I've never had this many requests for scientific material in such a short period of time." -Sean Whelan, PhD



and in nonhuman primates with colleagues in Montana-based NIH facilities - also were successful. If it proves as effective at preventing nasal infection in people as it is in animals, it may not only prevent infection but also curb transmission.

A few doors down, Ali H. Ellebedy, PhD, an assistant professor of pathology and immunology, was trying to generate antibodies that could be used as antiviral drugs. Using a SARS-CoV-2 protein made by Daved H. Fremont, PhD, a professor of pathology and immunology, Ellebedy injected mice, extracted antibody-producing immune cells, and then tested the antibodies' ability to neutralize the virus.

One antibody in particular was astonishingly potent, able to cure animals at minuscule doses. But it was still a mouse antibody. If it were given to people, the human immune system would recognize it as foreign and destroy it.

And then he got an email from a name he didn't recognize, at a biotechnology company he'd never worked with. Somehow they'd heard of his antibody, and they proposed a collaboration. Within two weeks, the company had fully "humanized" the antibody by changing its

genetic sequence to trick the human immune system into thinking it was human. With the help of Boon, Ellebedy is now testing whether the humanized version retains the potency of the original mouse antibody. If it does, it could quickly enter human clinical trials as a potential antiviral.

Inadequate diagnostic testing is part of the reason the pandemic took off in the U.S. The standard COVID-19 test involves inserting a long, thin swab uncomfortably deep into the nose. The swabs then are placed into a solution and processed. For much of this year, supplies of swabs and processing reagents were limited, making it hard to track the spread of the virus.

Milbrandt and Richard D. Head, a professor of genetics, led a highly skilled scientific team to develop a method for testing for viral RNA in saliva. The test, which received emergency use authorization from the FDA in August, requires only spitting into a cup, is highly sensitive to detecting even tiny levels of the virus, and returns a result in under a day. Washington University has adopted the saliva test to screen its undergraduates, and the state of Missouri is disseminating the testing platform statewide.

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work we did.

The battle continues

It has been a year since Whelan and Diamond first discussed an unnamed virus causing a tiny outbreak far away. The global pandemic still claims thousands of lives worldwide every day. And the researchers, physicians and other biomedical workers who have spent the past year battling that virus see no end in sight. "It's been pretty intense," Diamond said this past fall. "I haven't had a day off since January 2020. Not a single one. But the reward is not feeling helpless. We were the first to show intranasal vaccines work better than injectable ones. Even if our vaccine doesn't end up being the first one, any nasal vaccine will be based on the

"A lot of people, even a lot of scientists, are feeling a pang because they can't do anything. For us, it's exhausting, but our labs at Washington University are making a contribution. We're doing something. And that's worth a lot." \Box

Looking at plague assays stained with crystal violet, Pallavi Chandra, PhD, screens small molecules for activity against SARS-CoV-2. Chandra and Ekansh Mittal, PhD, both staff scientists, work in a biosafety level-3 lab headed by Jennifer A. Philips, MD, PhD.

Sequencing the future

Generous pledge from James and Elizabeth McDonnell accelerates the expansion of their namesake genome institute

BY MARY LEE

he Elizabeth H. and James S. McDonnell III Genome

Institute at Washington University School of Medicine has a storied history. Founded in 1993, the institute was a leader in the international effort to decode the human genome, contributing 25% of the completed DNA sequence. Institute investigators also were the first to map the genomes of cancer patients to reveal the genetic underpinnings of their tumors.

Through these and other initiatives supported by more than \$1.3 billion in research funding, the McDonnell Genome Institute (MGI) has played a key role in identifying genetic variants associated with disease and paving the way for the rise of personalized medicine.

Now, as MGI is poised to enter a new era of leadership, Elizabeth and James McDonnell, who endowed the institute with a \$25 million naming gift in 2015, have stepped forward with a new pledge to provide \$50 million in expendable funding. The commitment, through the JSM Charitable Trust, will accelerate plans to transform MGI that were announced earlier.

"Our vision involves bringing the institute's massive DNA sequencing resources to bear on the challenge of integrating precision medicine into standard medical practice for all patients," said David H. Perlmutter, MD, executive vice chancellor for medical affairs and the George and Carol Bauer Dean of the School of Medicine. "This magnanimous gift from Jim and Libby will pave the way. We are deeply grateful for their continued partnership in our efforts to expand the boundaries of genomics for the benefit of all."

Finding disease connections

The shift in MGI's focus is, in many respects, the result of its success in helping further the science of whole-genome sequencing and analysis. As the speed of sequencing has increased and the cost decreased over the past two decades, scientists around the world have read millions of genomes and cataloged hundreds of thousands of genetic alterations. But a significant number of these variations have no known connection to disease.

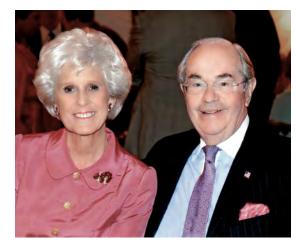
"Many are not dangerous, and some may be protective," said Jeffrey D. Milbrandt, MD, PhD, the James S. McDonnell Professor and head of the Department of Genetics, who is leading the transformation of MGI as its new executive director. "The major task before us is to separate the genomic wheat from the chaff. We must identify which variants are important and validate their function in disease. This is critical for the advancement of precision diagnostics and therapeutics."

Technology will play a key role in MGI's ability to expand its expertise in the functional genomics arena. Plans call for the addition of powerful tools to enable high-throughput testing of genomic sequence variants in model biological systems, including single-cell RNA sequencing instrumentation; CRISPR genome engineering technologies; mass spectrometry for the identification of proteins and metabolites; and quantitative imaging analysis.

Building powerful data sets

Of particular interest to the McDonnells, their gift will provide funding to conduct large-scale genome sequencing and analysis for patients with rare diseases and neurodevelopmental disorders at St. Louis Children's Hospital and patients at the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine. The information generated from this work, when combined with clinical information, will create rich data sets that can be mined for an array of research studies.

The McDonnells have been champions of pediatric and oncology research at Washington University Medical Center for many years. The couple lost their 2-year-old daughter, Peggy, to neuroblastoma, a common childhood cancer, in 1972.



"The technological wizardry we have today is unparalleled," Milbrandt said. "Twenty years ago, a multi-year, international effort first sequenced the human genome; today we can sequence the entire genome from a single cell in one day." The McDonnells' foresight in providing expendable funding will allow us to invest in equipment and infrastructure now, while this field is catching fire, so we can reap a powerful return later in the form of new discoveries and treatments."

The McDonnells' pledge also will support the recruitment of a visionary leadership team and other innovative investigators, including those who specialize in bioinformatics and computational biology. In addition, MGI will launch a master's degree program to prepare students interested in machine learning and artificial intelligence for careers in biology and genomics.

Elizabeth H. and James S. McDonnell III

"My mother died of cancer, and Libby has fought it as well," James McDonnell said. "Our experiences have motivated us to do whatever we can to fight the disease. We believe that experts across the university working together to apply genomic approaches to cancer and other disorders will bring about a healthier world."

Two additional pilot projects under consideration will evaluate whether genomic data collected from diverse populations of St. Louis residents can be leveraged to improve health and reduce health-care costs. These longitudinal studies, which would include underserved populations, could have longterm implications for community health.

"Large-scale genomic studies to date have focused mainly on people of European ancestry," Milbrandt said. "Our planned projects will help us broaden the reference human genome to people from all ancestries and ensure that the fruits of personalized medicine can be applied to all. We believe Washington University has a responsibility to be a leader in this area."

Extending a family legacy

The McDonnells' current pledge for MGI extends a family legacy of generosity that has had a significant impact at the School of Medicine, particularly in the area of genetics. James McDonnell's father, James S. McDonnell Jr., the founder of McDonnell Aircraft Corp., which later became McDonnell Douglas, provided funding to establish the James S. McDonnell Department of Genetics in 1975. The department now ranks among the best in the country. "The McDonnell family's influence on the medical school and the field of genetics is

"We believe that experts across the university working together to apply genomic approaches to cancer and other disorders will bring about a healthier world." – James S. McDonnell III

extraordinary," Milbrandt said. "They have always answered the call. Their gifts helped create a novel department, aided in the recruitment of exceptional faculty members who laid the groundwork for the university's participation in the Human Genome Project and have extended our excellence in the area of genomics."

Dean Perlmutter said the McDonnells' latest commitment will enable many groundbreaking discoveries. "Jim and Libby's gift will position our medical center as a unique leader in personalized medicine and a strong partner with our St. Louis community. Witnessing their approach to philanthropy and dedication to advancing human health has been one of the most inspiring experiences of my career."

The McDonnells hope their pledge will jumpstart MGI's transition."We are excited by the plans to take the institute to the next level," said James McDonnell, a member of the School of Medicine National Council, trustee of St. Louis Children's Hospital and of the St. Louis Children's Hospital Foundation and member of the Children's Discovery Institute Board of Managers. "We hope our gift motivates others to support the medical school's efforts."



James S. McDonnell Jr., (left) at the McDonnell Medical Sciences Building groundbreaking Sept. 30, 1967.

1950s

William "Bill" Reynolds, MD '56, was awarded an honorary doctorate of humane letters by the University of Montana.

1960s



Mordecai P. Blaustein, MD '61, is a professor of physiology and medicine at the University of Maryland School of Medicine. His work was noted in the European Heart

Journal and the Journal of General Physiology. Additionally, the third edition of a textbook he co-authored, "Cellular Physiology and Neurophysiology," was published in spring 2019.

Gerald Esparcia Jr., HA '62, has spent 12 years working with California prison healthcare centers, assisting with compliance in state law standard requirements.

Karen Wegener, GN '65, reports that, despite retiring nearly 20 years ago, she remains active in health care and has chaired the local hospital board for 15 years. She also was elected to the local ambulance board. She and her husband enjoy spending time with their three daughters, five grandchildren and three great-grandchildren.

H. Michael Jones, MD '66, was installed as president of the American Osler Society, a group dedicated to maintaining the legacy of Sir William Osler and his ideals in life and the practice of medicine. The group meets annually, centered around the presentation of papers on the history of medicine.

1970s

Curtis Gielow, HA '73, received the Civic Leader Award honoring his activism for patients and the profession of pharmacy during the 10th annual Next-Generation Pharmacist Awards Gala, sponsored by Pharmacy Times in conjunction with Parata Systems.



Dennis Bertram, MD '74, retired in 2014 as director of the Master of Public Health Program at the University of Buffalo School of Public Health and Health Professions. He now enjoys working in his art studio at Buffalo Arts Studio and exhibits regionally and nationally. His artwork can be viewed at dennisbertram.com.

Fred Horowitz, LA '76, DE '79, was elected to the Board of Directors of Access Health Ventures, LLC in Las Vegas. He also is a contributing author to the "CDT 2020 Coding Companion" textbook published by the American Dental Association.

1990s



Arnold Bullock, MD, HS '93, was honored with the Physician of the Year Award at the Christian Hospital Foundation Gala. He is a urologist at Christian Hospital and Washington University School of Medicine specializing in urologic oncology, male voiding and erectile dysfunction.

Marie Miller Howell, MS PT '93, is a board-certified geriatric clinical specialist and certified exercise expert for aging adults. She is self-employed in a Pilatesbased outpatient clinic focused on community fitness, aging adults and osteoporosis. She was expecting to earn a DPT in May 2020.



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Sharon Cresci, MD,

HS '95, led a committee that developed the American Heart Association's scientific statement on the potential for precision

medicine to improve treatment for patients with heart failure. She is an associate professor at the School of Medicine.



Douglas Pogue, MD '95, was named president of BJC Medical Group, a 600-provider group serving BJC HealthCare and Washington University.

John Lim, MD, HS '96, has published his first book, "How to Raise Your Child's Financial IO." It is a personal finance book geared for children. It is available as a free pdf download

at humbledollar.com/igbook as well as on Amazon in Kindle format.



Timothy Miller, MD/ PhD '98, the David Clayson Professor of Neurology at Washington University School of Medicine, and a group of his colleagues have received the inaugural

Healey Center International Prize for innovation in amyotrophic lateral sclerosis (ALS) research from the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital. The prize celebrates excellence in research by an individual or team that has made exceptional discoveries leading to a transformative advance in therapy development in ALS, also known as Lou Gehrig's disease.

Katherine Nowak, MS PT '99, EMBA '07, began a new position at Navvis Healthcare as market president for Missouri in January. She focuses on population health within value-based, health-care delivery models.



Katie Plax, MD '99, professor of pediatrics and director of the **Division of Adolescent** Medicine at Washington University School of Medicine, has received the Job Lewis Smith

Award for outstanding community service from the American Academy of Pediatrics.

The award, presented to Plax during the organization's annual conference in October, recognized her work as co-founder and medical director of the community-based health and social-services clinics called Supporting Positive Opportunities for Teens, more commonly known as The SPOT. The program has two locations: a free, drop-in center in St. Louis for those ages 13 to 24, and a school-based health center, The SPOT@Jennings, at Jennings High School in St. Louis County.

2000s

Laurie P. Shornick.

PhD '00, was named chair of the Department of Biology at Saint Louis University.

Mary Doi, MD '01, has been working at the U.S.

Food and Drug Administration for the past 10 years and enjoys her career in public health. She is working on data science projects as a lead physician in the Office of Translational Sciences in the Center for Drug Evaluation and Research.

Meredith Gronski, LA '03, OTD '05, OTR/L, CLA, was elected as president of the North Carolina Occupational Therapy Association. Her term as president-elect began July 1, 2018, and continues until 2021.



Timothy Loftus, MD

'06, has been working with the Florida Health Justice Project, an organization that advocates for healthcare access for Floridians, especially those in

vulnerable populations. He is in law school with plans to finish in May of 2021.



Adam Wende, PhD '06, was promoted

to associate professor at the University of Alabama at Birmingham. In addition to his professional update, Wende is a recent

survivor of leukemia, after being diagnosed in 2014, and has begun raising funds for

the Leukemia and Lymphoma Society. As a member of Team in Training, he is planning to run in the London Marathon in October 2021 to celebrate his survivorship and hopes to raise \$26,219. For more information on Wende's story, visit his Team in Training page at pages.lls.org/tnt/al/london21/awende.

Shirly Mildiner-Earley, PhD '07, is a clinical scientist at Calithera, a clinical-stage

biopharmaceutical company in San Francisco. 2010s

Jennifer Reeves, LA '09, MD '13,

completed a fellowship in family planning and started a position as assistant professor at Emory University School of Medicine, Department of Gynecology and Obstetrics, Division of Family Planning.

Alecia Vogel-Hammen, MD/PhD '13,

an instructor in child psychiatry at Washington University School of Medicine, has received the American Academy of

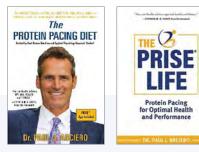
Child & Adolescent Psychiatry's 2019 Pilot Research Award for Attention Disorders. The award, supported by the academy's Elaine Schlosser Lewis Fund, provides up to \$15,000 in funding to junior faculty and child and adolescent psychiatry fellows interested in careers in child and adolescent mental health research.

Tamira Butler-Likely, PhD '14, soon will be a full-time entrepreneur operating a travel business, TNT Travels Group, and an editing business, Likely Write Editing.

Stephanie Wevrauch,

MSCI '15, DPT '15, has been named a 2019 Emerging Leader for the American Physical Therapy Association. The award recognizes a physical therapist who

has demonstrated extraordinary service, clinical passion and has made exceptional overall accomplishments and contributions to the physical therapy profession.



Paul J. Arciero, HS '94, reports that his book "The Protein Pacing Diet" is a No. 1 Amazon.com best-seller in three different categories and reached a high of No. 45 in Amazon's largest book category (over 3 million): weight loss/diet books. Women's World magazine also featured the book in November 2019. His newest book, "The PRISE Life," earned Amazon No. 1 new release and No. 5 best-seller. Additionally, Arciero was invited to present the Spring Nutrition Symposium at the New York Chiropractic College in March 2019. He is a professor in the Health and Human Physiological Sciences Department and director of the Human Nutrition, Performance & Metabolism Laboratory at Skidmore College.

the American Medical

Association (AMA) Women Physicians Section and the AMA Foundation to conduct a multicenter study of gender factors that may influence students' decisions to pursue careers in orthopedic surgery.

> Tayler Sheahan, PhD '17, and David Baranger, PhD '18, were married March 29, 2019, by friend and officiant Molly Stanley, PhD '17. The couple met at Washington

University while working on their PhDs in neuroscience. They are postdoctoral researchers at the University of Pittsburgh.

Razeena Umrani, DPT '18, recently completed a residency and fellowship at Houston Methodist Hospital, an accredited physical therapy acute care program.

OBITUARIES



Barbara Geller, MD, an emerita professor of child psychiatry in the Department of Psychiatry at the School of Medicine, died Friday, May 8, 2020, in hospice in St. Louis after a brief illness. She was 81.

A leading researcher in manic and depressive disorders in children, Geller received the first National Institutes of Health (NIH) research grant award to study mania during childhood. She also was the lead investigator on the multisite project Treatment of Early Age Mania (TEAM), the first large-scale, federally funded study of

drug treatments for childhood mania.

"She was a fiercely independent woman and a strong-minded thinker who achieved great academic success at a time when not many women had significant positions in science," said Joan L. Luby, MD, the Samuel and Mae S. Ludwig Professor of Psychiatry and director of the university's Early Emotional Development Program.

Geller pioneered studies of the effects of antidepressant drugs on children and adolescents, as well as pharmacologic studies of lithium for bipolar disorder in childhood. More than 100 researchers from universities around the world trained with Geller to learn about her research methods for diagnosing mania in childhood, as well as to learn how to use her adapted version of a standardized, child psychiatric interview.

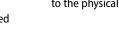


Ann J. Johanson, MD, a pioneer in the clinical use of human growth hormone, died in her home in Sanibel, Fla., Jan. 30, 2020. Johanson was born July 19, 1934, in St. Louis. She was a fifthgeneration physician dating back to her Norwegian forebearers. Johanson was 85.

Johanson received a bachelor's degree with honors from Washington University in St. Louis in 1956. As a pre-med student who majored in physical education and lettered in varsity basketball, volleyball, softball and field hockey, Johanson earned the Phoenix Award for the most outstanding female athlete. She attended medical school at the University of Missouri-Columbia — one of only three female graduates in her class — graduating with top honors in 1962. She completed an internship at the University of Minnesota, a residency at St. Louis Children's Hospital and a fellowship in endocrinology at Johns Hopkins Hospital in Baltimore. Then, she joined the University of Virginia where she became the first female full professor in pediatrics and developed a pediatric endocrinology division at the University of Virginia Medical Center.

She gained an international reputation in the field of growth disorders, specifically short-stature syndromes. Johanson and her partner, Robert M. Blizzard, MD, described, and therefore had named after them, the endocrine disorder Johanson-Blizzard Syndrome. Johanson eventually left academic medicine to head the human growth hormone division at Genentech Corporation in San Francisco. She became the first woman endocrinology director and was key to the breakthrough development and clinical use of rhGH, or synthetic recombinant human growth hormone. Thereafter, the lives of children deficient in growth hormone improved significantly because the supply of treatment medication was no longer limited by the scant amounts of human pituitary hormone that could be obtained at autopsy.

A longstanding supporter of the university, Johanson was passionate about funding scholarships. She is remembered as an exceptionally compassionate, dedicated physician with uncommon humility. She is survived by nephews Erik, Stephen and Peter, niece Kristen and their spouses and children, her sister in-law Kathren, as well as her close cousins Dr. Stephen Achuff, his spouse Cary and children, Elise, Jeannie, and Charlie and the Witherspoon family.









Cara Cipriano, MSCI '17, assistant professor of orthopedic surgery at the School of Medicine, and Kate Gerull, MD '20, received a grant from



Taevin Symone Lewis, **OT**, a recent graduate of the Program in Occupational Therapy at the School of Medicine, died Jan. 1, 2020, in a motor vehicle accident in St. Louis. She was 26.

Lewis was born in Greenwood, Miss., and later moved to Memphis, Tenn. She was the first to enroll in a cooperative degreeconferring program involving Harris-Stowe State University and Washington University. The program allowed her to earn a bachelor's degree in biology from Harris-Stowe in three years, followed by a master's degree in occupational therapy (OT) from Washington University in two years.

"Taevin was a trailblazer, paving the way for us to dedicate ourselves to increase diversity and inclusion in the profession," said Lisa Tabor Connor, PhD, executive director of the Program in Occupational Therapy.

Duana Russell-Thomas, OTD, a clinical specialist who worked with Lewis, said: "She was illumination, using her smile, honesty and passion to push herself and those around her to excellence. She was love, always seeing and serving those in need and setting the expectation to continue that work as a part of her career."

Lewis served in a wide range of activities, including: student government association's president and vice president at Harris-Stowe; 2016-17 Miss Black Missouri U.S. ambassador; tutor for St. Louis high school students; and volunteer for a sickle cell support group at St. Louis Children's Hospital.

On her LinkedIn page, she wrote: "I strive to be a woman of valor, a world shaker, a history maker."

She is survived by her father, Calvin Lewis (Aubra Lewis); mother, Quadril Siggers-Abron (Darron Abron); brothers Tevin, Nicholas, Kylan, Kyler and Keaton; grandmothers Minnie Lewis and Deborah Siggers; and grandfather, Walter Bibbs.



Momoko Oyama, a rising third-year student at the School of Medicine, died Sunday, June 14, 2020, at her St. Louis apartment. Oyama,

who had planned to become a neonatologist, was 24.

"Momo was kind, smart and generous with her time," said Lisa Moscoso, MD, PhD, professor of pediatrics and associate dean for student affairs at the School of Medicine. "She really found meaning and joy in her work with children, and her playful laughter and quiet patience were traits we love to see in pediatrics.

"Her loss is devastating to her family, her class and the many other people who loved her — and it's also a great loss to the young patients and families she would have helped as a physician. She genuinely delighted in children and would have been an amazing addition to the field of pediatrics."

Oyama was born in Fukuoka, Japan, and moved to the U.S. when she was 3. Growing up in St. Louis, she attended Japanese school on Saturdays and was fluent in Japanese. She graduated from Washington University in 2018 with a bachelor's degree in anthropology and a minor in biology from Arts & Sciences. While an undergrad, she participated in the Institute for Public Health's Summer Research Program, which she credited with sparking her interest in public health.

Oyama is survived by her mother, Reiko Oyama, director of nuclear pharmacy at the university's Mallinckrodt Institute of Radiology; her father, Nobuyuki Oyama; her sister, Sakura Oyama (Oliver McMillan); and her beloved dog, Kuma.



Karen Seibert, PhD, a deeply respected leader in pharmacology

at the School of Medicine, died Monday, Nov. 9, 2020, at her home in Chesterfield, Mo., after a battle with a cancer. She was 61. Seibert wore many hats in her long, successful career. She was the founding executive director of the Center for Clinical Pharmacology, a formal collaboration between Washington University and the University of Health Sciences & Pharmacy. In addition to that role, she was a professor of anesthesiology, of

pathology and immunology, and of genetics at the School of Medicine. Further, she was associate director of shared resources for Siteman Cancer Center, in conjunction with Washington University and BJC HealthCare.

Seibert also had leadership roles in research collaborations between Washington University and the biopharmaceutical company Pfizer Inc., and the university and Mallinckrodt Pharmaceuticals. The collaborations were established to provide opportunities for academic researchers to translate and transform concepts into breakthroughs leading to drug discovery.

"As anyone who knew Karen can appreciate, she was a true force of nature brilliant with a deeply inquisitive mind, a wonderful sense of humor, and a remarkable ability to bring people together and form partnerships," said Michael Avidan, MBBCh, the Dr. Seymour and Rose T. Brown Professor of Anesthesiology and head of the Department of Anesthesiology.

Before Seibert took on her role at the center, she developed and led the clinical genomics group known as Genomics and Pathology Services at the School of Medicine. There, she led an effort to develop genomic-based clinical tests for use in the diagnosis and treatment of patients with cancer and other diseases.

Before joining the faculty in 2010, she spent nearly 20 years in the pharmaceutical industry, at Pfizer Inc. Her first 10 years were devoted to the development of the arthritis pain-relief drug Celebrex. She became a vice president of research and development for Pfizer's St. Louis labs and led searches for new treatments for arthritis, heart disease, diabetes and other conditions.

She came to Pfizer after working as a Washington University postdoctoral fellow in the lab of Philip Needleman, PhD, not long before his group identified an enzyme known as COX-2 that produces pro-inflammatory prostaglandins. They showed that COX-2 is a critical component in processes that cause inflammation and pain. Celebrex is a COX-2 inhibitor.

Seibert earned a bachelor's degree in biological sciences from Northwestern University, a master's in pharmacology from the University of Toledo College of Pharmacy and a doctorate from Vanderbilt University School of Medicine.

She received numerous honors over her career and was so highly regarded that Siteman Cancer Center renamed her position there, in perpetuity, the Karen Seibert Associate Director of Shared Resources. Also, before her death she was informed that Siteman had created the Karen Seibert Lifetime Achievement Award and that she was its first recipient.

Seibert is survived by her husband, Robert Boyd; sister, Kathryn Howe (James); mother-in-law, Rosemary Boyd; and numerous in-laws, nephews, nieces and friends.

1940s

Donald T. Behrens, MD '48; Feb. '20 Joseph S. Bierman, LA '45, MD '50; May '20 David Feldman, MD '43; March '20 Evelyn Beck Goldberg, OT '47; Jan. '20 Fred P. Handler, MD '47; April '20 Carl W. Hill, HS; May '20 Mary Jane Hirstein, NU '48; Oct. '19 John O. Kildow, MD '48; Jan. '20 Stanley L. London, MD '49; June '20 Carlyle A. Luer, MD '46; Nov. '19 Helen B. Paust, NU '48; May '20 Leonard W. Ritzmann, MD '45; Oct. '19

Maurice L. Sievers, MD '49; Jan. '20

Mary K. Thomas, NU '47; Feb. '20

1950s

Beatrice Borenstein, OT '53; Nov. '19 Donald L. Bornstein, HS '55; April '20 William L. Brydon, MD '56; June '20 Roy J. Buehrle Jr., DE '50; Nov. '19 Sharon Burritt, NU '50; March '20 Johanna B. Butt, NU '51; Feb. '20 Virginia L. Dancy, NU '52; Jan. '20 Marilyn Jane Danforth, NU '52; April '20 Edgar Draper, LA '46, MD '53; Nov. '19 Benjamin Emanuel, HS; Oct. '19 Lela Gilmer, NU '53; Nov. '19 William I. Goettman, MD '58; Oct. '19 Marcy A. Goldstein, MD '51; Oct. '19 JoAnn Hagedorn, NU '55; Dec. '19 Hadley H. Hasemeier, DE '51; Dec. '19 Gilbert Hermann, MD '54; March '20 Allan E. Kolker, LA '54, MD '57; March '20 John C. Lemon, MD '55, HS '58; Sept. '19 Edward Lewin, MD '55, HS; April '20 Malcolm R. Lewis, LA '48, MD '52; Nov. '19 Charlotte W. Malotky, NU '50; April '20 Nancy Massholder, OT '56; Jan. '20 Robert C. Meredith, MD '57; Oct. '19 Noboru Oishi, LA '49, MD '53; March '20

Robert J. Robertson, DE '58; May '20 Shirley E. Shearman, NU '52; Feb. '20 Joel L. Siner, MD '53; May '20 Larry L. Weiss, HS; Nov. '19 Lorna Marshall Wilson, NU '53; Aug. '19 James F. Wittmer, LA '55, MD '57; June '20 Diane R. Worthington, NU '55; Nov. '19

1960s

George S. Allen, MD '67; Dec. '19 Javad Arasteh, HS '62; April '20 J. Thomas Bradley, DE '67; Oct. '19 John P. Christy, LA '59, MD '63; March '20 Lyman B. Fogg, MD '60; Nov. '19 Elliot F. Gellman, HS '63; Jan. '20 James R. Goggin, MD '62; April '20 Alan L. Goldman, MD '63; April '20 Joan M. Gornik, PACS '67; Jan. '20 Richard H. Jacobsen, MD '62; April '20 Charles A. Janda, HS '64; Sept. '19 A. Victor Khayat, HS '60; Feb. '20 Benedicto P. Mariano, HS '65; Dec. '19 John D. Morgan, MD '61; April '20 Norman D. Nelson, MD '66; May '20 William L. Phelps, HS; Nov. '19 Eugenia T. Poulos, HS; March '20 **Emanuel Rashet,** HS; June '20 George F. Reinhardt, LA '60, MD '64; Dec. '19 William G. Ridgeway, HS '67; April '20 Peter Rosen, MD '60; Nov. '19 Eugene J. Sayfie, MD '60; May '20 John J. Sheridan, MD '69, HS '74; April '20 John E. Staples, DE '63; Jan. '20 **D. Reid Tickle,** HS '60; Dec. '19 Don E. Williams, DE '65; April '20

1970s

Ronald Shizuo Arakawa, DE '79; April '20 Joanne Black, OT '71; March '20 Alan Huber Broadbent, DE '75; April '20 Kenneth D. Delp, DE '71; Sept. '19 Edgar Draper, LA '60, HS '70; Nov. '19 Andrew Jay Drexler, HS '78; Nov. '19 Richard Morgan Frederick, DE '74; Nov. '19 Daniel Dennis Heer, DE '75; March '20 Jerrold Asao Hiura, DE '76; Dec. '19 Margaret A. Kitchell, MD '74; March '20 **S. Robert Kovac,** LA '60, HS '70; Dec. '19 Barry Joseph Kraynack, HS '74; June '20 Michael Frederick Lyons, DE '78; Sept. '19 Michael L. O'Brien, DE '70; April '20 Lourdes C. Pineda, HS '74; March '20 Daniel Jose Santa Cruz, HS '77; March '20 Robert Eliot Silverman, MD '78, PhD '78; June '20 Charles N. Swisher, HS '72; May '20 Ronald P. Wilbois, HS '71; May '20

1980s

Marc Russell Kamp, DE '86; Feb. '20 Daniel J. LaMar, HS '85; March '20 James R. Panuska, HS '86; April '20

1990s

David Carl Chiara, MD/PhD '97; Sept. '19

2010s

Kasey Marie Hess, OT '10; Dec. '19

In Memorium

To read full obituaries on any of the alumni listed on this page or to submit an obituary for publication in a future issue of Outlook magazine, visit medicalalumni.wustl.edu/alumni.



Bill Danforth: A tribute

Current dean of the medical school remembers his predecessor

ost people know Bill Danforth as one of the longestserving university chancellors in the country, and as a dedicated civic leader and philanthropist, but for me, Bill Danforth was first and foremost a physician and a scientist. These early choices — to go to medical school, to start his professional life as a physician in the Navy during the Korean War, to return to St. Louis to join the Washington University cardiology faculty — were the first in a series of decisions that had as their common denominator the desire to help people, to be of service to his fellow man and to his nation, and to leave our university, our city, and the world better than he found them.

As he served first as executive vice chancellor of medical affairs for years before taking on the chancellor experience, Bill had a deep understanding of the unique and complementary strengths of the two campuses. In both roles he worked to bridge both the geographic and cultural divides that inevitably arise between medical schools and the rest of the university. He knew that Washington University would only be as strong as its weakest link and also knew that a strong medical school would strengthen the rest of the university, which in turn would strengthen the Medical Campus — a virtuous cycle.

As chancellor, he increased funding for basic and medical research, laying the foundation for so many of the School of Medicine's incredible achievements. I feel his impact every day in the depth of talent and intellectual activities that have distinguished our school and our university. It could only have happened from decades of Bill recognizing, nurturing and empowering the right people and as a result of his firm devotion to the importance of quality in thinking. On more than one occasion he talked with me about his deep belief in "academic decision-making" and somehow, I knew that meant that consideration of what was good for our core missions — patient care, education and research — had to be a part of every decision. I was so fortunate to have had some time with him over these last several years, moments that I will always treasure. One night we had several minutes alone before

a big dinner event. I was recounting some of the things that I had learned from my mentors and we landed on a discussion of how important it was to encourage "big" thinking. He told me that when he was a boy, his grandfathe asked him to get the dictionary and find the page with the word "impossible." And then he was told to tear that page out and throw it away.

He understood that in an academic setting, and in a city, change for the better takes time, patience and perseverance to build a community and a culture with a shared sense of direction and aspirations.

In a word, his was leadership based on commitment. A

A cardiologist by training, Bill Danforth joined the School of Medicine faculty in 1957.

commitment that began in the halls of the Medical Campus when he decided to pursue a profession that is all about helping one's fellow human beings, and one that took as its specific, fortunate object our university and its place in our region. He understood that commitment means believing that there is no limit to what you can accomplish and that, at the same time, accomplishment is always incremental, that we must strengthen and take seriously every individual and every school that together make our institution great. He put in the time and the commitment, and we are all the better for it. Bill Danforth was tall in stature and presence but gigantic in impact. It is hard to fathom how one person could have fostered so much good in the people around him. His style of leadership and the mark he made on this university live on in all of us.

> — David H. Perlmutter, MD, executive vice chancellor for medical affairs and the George and Carol Bauer Dean of the School of Medicine



William H. Danforth II, MD, chancellor emeritus of Washington University and founding chair of the Donald Danforth Plant Science Center, died at his home on Wednesday, Sept. 16, 2020. He was 94.

Danforth graduated from Harvard Medical School in 1951 and completed an internship in medicine in 1952 at Barnes Hospital. After two years as a Navy doctor during the Korean War, he returned to Washington University and never left.

A cardiologist, he joined the School of Medicine faculty in 1957 after completing residencies in medicine and pediatrics at Barnes and St. Louis Children's hospitals, respectively.

At age 39, he was appointed vice chancellor for medical affairs and president of the Washington University Medical Center in 1965. He was named a full professor of internal medicine in 1967.

As vice chancellor, Danforth stood beside and gave counsel to Chancellor Thomas Eliot during the student unrest of the 1960s and was the universal choice in 1971 for 13th chancellor when Eliot retired.

During Danforth's chancellorship from 1971 to 1995, Washington University grew in national and international recognition for its teaching and research. The university strengthened its academic programs, significantly expanded resources for scholarship and scientific discovery, and completed its transition from a local college to a national research university.

By the time he retired as chancellor in 1995 and became chair of Washington University's Board of Trustees, his list of accomplishments included the establishment of 70 new endowed faculty professorships; construction of dozens of new buildings; tripling the number of student scholarships; and growth of the endowment to \$1.72 billion, which at the time was the seventh largest in the country.

Washington University's Hilltop Campus was renamed the Danforth Campus in 2006 in recognition of his and his family's contributions to the university.

To read more about Danforth's legacy and reflections from the university community, visit: rememberingbilldanforth.wustl.edu.



Bringing lifesaving treatment to Guatemala's only cancer clinic for the poor

BY TAMARA BHANDARI

Prior to the pandemic, the School of Medicine spearheaded a binational collaboration to install and calibrate an advanced radiation therapy machine, the Halcyon, at the Instituto Nacional de Cáncerologia (INCAN; National Cancer Institute) in Guatemala.

In a country of 17 million where cancer is the third leading cause of death, only INCAN treats the poor. Patients are treated on a first-come, first-served basis and waiting rooms quickly fill up. In resource-limited settings, radiation therapy is often the best cancer treatment option. The Halcyon provided a much-needed equipment boost as the institute's existing machines were either unsuited for cervical or breast cancer, the two most commonly seen cancers in the population, or emitted such weak radiation that a typical 10-minute treatment took closer to an hour.

INCAN has continued treating patients throughout the pandemic, despite a nationwide nightly curfew for several months and limited bus service that makes the daily trips to the clinic challenging for patients and staff. More than 300 patients were treated on the new Halcyon machine in its first year of operation. For about four months in the summer and fall of 2020, one of INCAN's other radiotherapy machines was out of commission and another was only partially functional. Without the Halcyon, INCAN's doctors would have had to refuse or delay care for dozens of cancer patients.

Read more about how WashU Medicine is improving cancer treatment in Guatemala at outlook.wustl.edu/guatemala. Washington University School of Medicine Office of Medical Public Affairs MS 8508-29-12700 660 S. Euclid Ave. St. Louis, MO 63110-1010

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Pandemic milestone

(Top) Joan Niehoff, MD, an associate professor of anesthesiology, receives a COVID-19 vaccination, as WashU Medicine and BJC HealthCare begin administering the first round of vaccines to older health-care workers and those in direct contact with infected patients. (Bottom) The face of pure relief.