

Outlook



Washington
University in St. Louis

SCHOOL OF MEDICINE

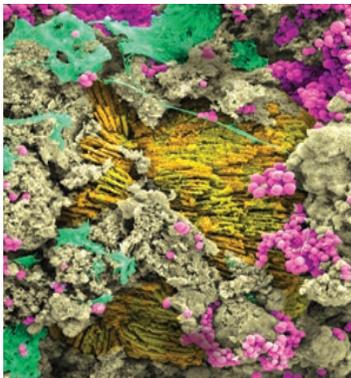
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AUTUMN 2017

SEEING THE Invisible

Cellular imaging facility reshapes
biomedical research





MATTHEW JOENS (WUCCO) AND JEN WALKER (HUTGREN LAB)

COVER Center for Cellular Imaging equipment reveals *Staphylococcus aureus* bacteria (purple) on the surface of a catheter. The bacteria release the enzyme urease, which hydrolyzes urea resulting in crystal formation (gold) and the protein fibrinogen (teal). This helps protect the bacteria from immune cells (tan) and antibiotics. See page 21.

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A new book sheds light on how medical center visionaries helped save the neighboring Central West End.

14 Inside an epidemic

In surveying some 25,000 addicts, psychiatrist Ted Cicero, PhD, has uncovered a series of factors leading to the current U.S. opioid crisis.

21 Making the invisible visible

To keep Washington University at the forefront of biomedical research, a one-stop shop provides access to the most sophisticated microscopes, plus professional guidance in experimental design, sample preparation and data analysis.



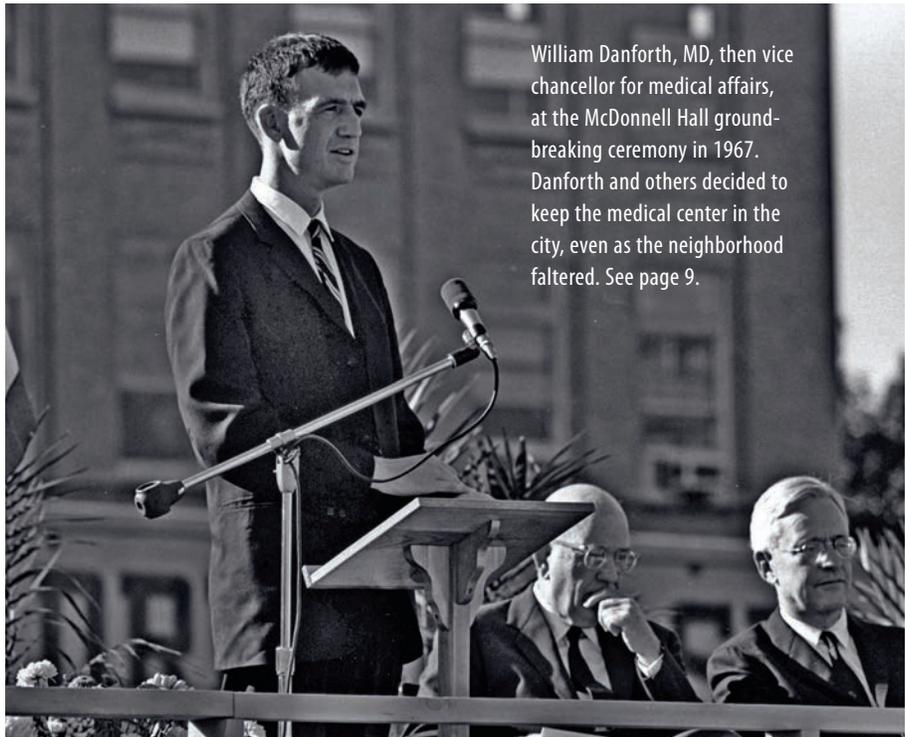
Park rangers in Missouri are joining the fight against the opioid epidemic. Above, rangers listen as David Tan, MD, chief of the emergency medical services section, talks about the crisis. Increasingly, overdoses are occurring in public parks. See page 14.

TIM PARKER

Outlook

Washington University School of Medicine

OUTLOOK.WUSTL.EDU AUTUMN 2017



William Danforth, MD, then vice chancellor for medical affairs, at the McDonnell Hall ground-breaking ceremony in 1967. Danforth and others decided to keep the medical center in the city, even as the neighborhood faltered. See page 9.

BERNARD BECKER MEDICAL ARCHIVES

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GETTY IMAGES

The Department of Ophthalmology has been renamed in honor of John F. Hardesty, MD. A \$10 million gift from his daughter is funding research and patient care and recognizing Hardesty's legacy of service. See page 30.

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Alzheimer's, sleep connection

Poor sleep leads to increase in Alzheimer's-related brain proteins

Disrupting just one night of sleep in healthy, middle-aged adults causes an increase in amyloid beta, a brain protein associated with Alzheimer's disease, according to a study from the School of Medicine, Radboud University Medical Centre in the Netherlands and Stanford University. And a week of tossing and turning leads to an increase in tau, another brain protein that has been linked to Alzheimer's and other neurological diseases.

"We think that perhaps chronic poor sleep during middle age may increase the risk of Alzheimer's later in life," said David M. Holtzman, MD, the Andrew B. and Gretchen P. Jones Professor, head of the Department of Neurology and the study's senior author. These findings were published July 10 in the journal *Brain*.

For this study, 17 healthy adults ages 35 to 65 with no sleep problems or cognitive impairments wore a wrist activity monitor for up to two weeks, which measured how much time they spent sleeping.

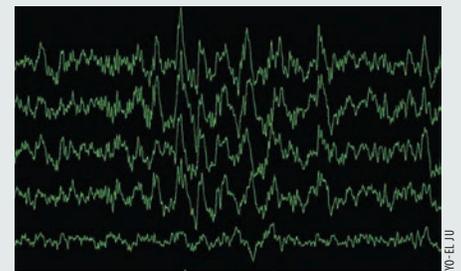
Each participant also spent a night in sleep rooms at the medical school, where they wore headphones over the ears and

scalp electrodes to monitor brain waves. Half the participants were assigned to have their sleep disrupted during the night. Every time their brain signals settled into the slow-wave pattern characteristic of deep, dreamless sleep, the researchers sent a series of beeps through the headphones, gradually getting louder, until the participants' slow-wave patterns dissipated and they entered shallower sleep.

Slow-wave sleep is when neurons rest and the brain clears away the molecular byproducts of mental activity.

The next morning, the participants who had been beeped out of slow-wave sleep reported feeling tired and unrefreshed, even though they had slept just as long as usual. Each underwent a spinal tap so the researchers could measure the levels of amyloid beta and tau in the fluid surrounding the brain and spinal cord.

A month or more later, the process was repeated, except that those who had their sleep disrupted were allowed to sleep through the night undisturbed, and those who had slept uninterrupted were disturbed by beeps.



Brain waves during slow-wave sleep, measured as a study participant slept.

The researchers compared participants' amyloid beta and tau levels after the disrupted night to the levels after the uninterrupted night. They found a 10 percent increase in amyloid beta levels after a single night of interrupted sleep, but no corresponding increase in tau levels. However, participants whose activity monitors showed they had slept poorly at home for the week before the spinal tap showed a spike in tau levels.

Yo-Ei Ju, MD, co-first author and an assistant professor of neurology, said it is unlikely that a night or even a week of poor sleep has much effect on overall risk of developing the disease. "The main concern is people who have chronic sleep problems," Ju said.

Study: Ketamine does not reduce postoperative pain

To blunt postoperative pain and reduce the need for opioid drugs following surgery, anesthesiologists often give patients low doses of the drug ketamine during operations.

But a new study led by anesthesiologists at the School of Medicine and the University of Michigan Medical School indicates that ketamine doesn't lower pain levels or reduce the need for pain-killing opioid drugs in the days after an operation. Further, older patients who receive ketamine during surgery are more likely to experience hallucinations

and nightmares in the recovery room and for several days following surgery.

The findings are published online May 30 in the journal *The Lancet*.

"We found that the current practice of



Anesthesiologists routinely give surgery patients low doses of the drug ketamine.

giving low doses of ketamine to patients during surgery is not having the desired effect," said first author Michael S. Avidan, MBBCh, the Dr. Seymour and Rose T. Brown Professor of Anesthesiology at Washington University. "So we need to determine whether higher doses might be more effective, or we need to find alternatives to opioids."

Avidan, with co-principal investigator George A. Mashour, MD, PhD, an anesthesiology professor at the University of Michigan Medical School, led a study aimed at evaluating ketamine as a way to prevent delirium and other complications. In previous research, Avidan had found that up to 20 percent of older patients experienced delirium following surgery.

The researchers followed 672 surgery patients in four countries: the U.S., Canada, India and South Korea. During surgery, the patients — all at least 60 years of age — either received no ketamine, a very low dose of the drug, or a slightly higher dose. The doses of ketamine given in the study are the doses routinely given to surgery patients by anesthesiologists who want to lower patients' levels of postoperative pain.

Avidan said the fact that the study results were consistent at different sites in different countries makes him confident that current ketamine practices are not having the desired effect on delirium and postoperative pain. He said clinicians should reconsider the common practice of giving low doses of ketamine during surgery.



EMPOWERING WOMEN Incoming female residents in internal medicine gather for a networking event sponsored by the Forum for Women in Internal Medicine (FWIM). Created in 2014, FWIM supports the professional and personal development of women trainees in the Department of Medicine. The group hosts career workshops and lectures, facilitates mentoring opportunities and fosters a sense of camaraderie.

To learn more, visit ghs.wustl.edu/fwim.html

Klein to head PhD training program

Robyn S. Klein, MD, PhD, a physician-scientist recognized internationally for her work on the brain's immune system, has been named vice provost and associate dean for graduate education for the Division of Biology & Biomedical Sciences (DBBS), effective Jan. 1.

Klein succeeds John H. Russell, PhD, who is retiring but will retain an appointment in developmental biology, and plans to revitalize the Office of Postdoctoral Affairs.

Widely emulated for its interdisciplinary approach to training PhD scientists, DBBS crosses both the Danforth and Medical campuses. It brings together about 525 faculty members from 37 departments in the School of Medicine, Arts & Sciences and the School of Engineering & Applied Science who teach and mentor some 500 graduate students, making it the largest PhD program at the university.

As associate dean, Klein will set the direction of graduate education at DBBS. She also will be the first associate dean of graduate education to hold the title of vice provost, a change in governance that recognizes the status of DBBS as a universitywide academic endeavor. Klein intends to build on the division's strength in training young scientists, and to prepare students for interdisciplinary careers that extend beyond academic domains. Klein also plans to increase recruitment of underrepresented students.



Robyn S. Klein, MD, PhD



ROBERT BOSTON

(From left) Davis, Johanson, Carothers and Grange.

Boy meets doctor who named his rare condition

Matthew Carothers, 13, a patient with Johanson-Blizzard syndrome, recently met the doctor who discovered the extremely rare congenital condition. Short and thin for his age, Carothers first came to Washington University at age 5 for thyroid problems. Geneticist Kathy Grange, MD, a professor of pediatrics, recognized the syndrome, which causes pancreatic insufficiency. With diagnosis and treatment, his quality of life has greatly improved. Over the years, Grange said she wished she could discuss Carothers' medical issues with Ann Johanson, MD, who co-named the syndrome with mentor Robert Blizzard, MD, in 1972. Unbeknownst to Grange, Johanson was living in the St. Louis area. Upon realizing this through Facebook connections, nurse practitioner Susan Davis invited Johanson to the Medical Campus.



NEW ACADEMY MEMBERS In recognition of their distinguished achievements in original research, L. David Sibley, PhD (left), and David C. Van Essen, PhD, recently were elected to the National Academy of Sciences. Election is considered one of the highest honors accorded a U.S. scientist or engineer. Sibley, the Alan A. and Edith L. Wolff Distinguished Professor of Molecular Microbiology, is an expert on the cellular microbiology of parasites. Van Essen, the Alumni Endowed Professor of Neurobiology, studies the structure, function, development and evolution of the cerebral cortex.

Study links intestinal viruses to diabetes

A child's chance of developing Type 1 diabetes may be influenced by the viruses that live in his or her gut, according to a new study.

"We identified one virus that was significantly associated with reduced risk, and another group of viruses that was associated with increased risk of developing antibodies against the children's

own cells," said Herbert "Skip" Virgin IV, MD, PhD, the Edward Mallinckrodt Professor and head of Pathology and Immunology, and the study's senior author. "It looks like the balance of these two groups of viruses may control the risk of developing the antibodies that can lead to Type 1 diabetes."

The findings suggest a way to predict, and maybe even prevent, the life-altering diagnosis.

Type 1 diabetes develops as a two-step process. First, people acquire antibodies against their own pancreatic cells responsible for producing insulin, a hormone that allows cells to absorb sugar from the bloodstream. Some children generate the auto-antibodies but never develop disease.

In other children, however, the auto-antibodies signal an attack by the body's own immune system on the pancreas that leads to Type 1 diabetes.

Virgin and colleagues examined stool samples obtained from birth to age 3 from children whose genes put them at high risk of developing Type 1 diabetes. They matched 11 children who went on to acquire auto-antibodies — five of whom later developed Type 1 diabetes — with 11 children who did not develop auto-antibodies or the disease.

A previously unknown virus related to circoviruses was found in five of the 11 children who did not develop auto-antibodies, but not in any of the children who did.

The researchers also found differences in a group of viruses called bacteriophages that infect bacteria, not human cells. Children carrying bacteriophages that target the *Bacteroides* species — one of the major groups of intestinal bacteria — were more likely to start down the path toward diabetes.



ROBERT BOSTON

Herbert "Skip" Virgin IV, MD, PhD, talks with post-doctoral researcher Dale Balce, PhD.



Millions of Americans take proton pump inhibitors for heartburn, ulcers and other gastrointestinal problems.

Popular heartburn drugs tied to higher death risk

Risk increases the longer the drugs are used

Popular heartburn drugs called proton pump inhibitors (PPIs) are linked to a higher death risk, a new study shows. This risk increases the longer the drugs are used.

The research is published online July 3 in the journal *BMJ Open*.

Doctors widely prescribe PPIs to treat ulcers and other gastrointestinal problems. PPIs, under brand names such as Prevacid, Prilosec and Nexium, also are available over the counter. Both PPIs and H2 blockers, another class of drug, are prescribed for serious medical conditions such as upper gastrointestinal tract bleeding, gastroesophageal reflux disease and esophageal cancer.

A kidney doctor by profession, senior author Ziyad Al-Aly, MD, previously has published studies linking PPIs to kidney disease. Studies from unrelated groups have associated PPI use with health problems ranging from bone fractures to dementia.

Al-Aly, first author Yan Xie, PhD, a data scientist, and colleagues reasoned that, cumulatively, these side effects may affect the mortality rate of PPI users.

To find out, the researchers sifted through millions of de-identified veterans' medical records in a database maintained by the U.S. Department of Veterans Affairs. They identified 275,933 people who had been prescribed a PPI and 73,355 people prescribed an H2 blocker between October 2006 and September 2008, and noted how many died and when over the following five years.

"No matter how we sliced and diced the data from this large data set, we saw the same thing: There's an increased risk of death among PPI users," said Al-Aly.

Al-Aly and colleagues found a 25 percent increased risk of death in the PPI group compared with the H2 blocker group. Among people taking the drugs for one to two years,

the risk to PPI users was nearly 50 percent higher than that of H2 blocker users.

The researchers estimate that, for every 500 people taking PPIs for a year, there is one extra death that would not otherwise have occurred.

Although the recommended treatment regimen for most PPIs is short — two to eight weeks for ulcers, for example — many people end up taking the drugs for months or years.

"A lot of times people get prescribed PPIs for a good medical reason, but then doctors don't stop it and patients just keep getting refill after refill after refill," Al-Aly said. "There needs to be periodic re-assessments as to whether people need to be on these."

Over-the-counter PPIs contain the same compounds as prescription PPIs, just at lower doses. The Food and Drug Administration recommends taking PPIs no longer than four weeks before consulting a doctor.

Flavonoids are commonly found in foods such as black tea, red wine and blueberries.



GETTY IMAGES

Gut microbes, flavonoids protect against severe flu

A new study shows that a particular gut microbe can prevent severe flu infections in mice, likely by breaking down naturally occurring compounds — called flavonoids — commonly found in foods such as black tea, red wine and blueberries.

The research, conducted in mice by School of Medicine scientists, also indicates that this strategy is effective in staving off severe flu damage when the interaction occurs prior to infection with the virus. This work also could help explain the wide variation in human responses to influenza infection.

The study is published in the journal *Science*.

“For years, flavonoids have been thought to have protective properties that help regulate the immune system to fight infections,” said first author Ashley L. Steed, MD, PhD, an instructor in pediatrics who treats intensive care patients at St. Louis Children’s Hospital.

Previous evidence suggests that the gut microbiome may be important in protecting against severe influenza infections, so in this study, the researchers aimed to identify just what gut microbes might provide that protection.

“We were able to identify at least one type of bacteria that uses these dietary compounds to boost interferon, a signaling molecule that aids the immune response,” said the study’s senior author, Thaddeus S. Stappenbeck, MD, PhD, the Conan Professor of Pathology & Immunology.

This prevented influenza-related lung damage in the mice. It is this kind of damage that often causes significant complications such as pneumonia in people.

As part of the study, the researchers screened human gut microbes looking for one that metabolized flavonoids. Stappenbeck and Steed identified one such microbe that they suspected might protect against flu damage.

The microbe, called *Clostridium orbiscindens*, degrades flavonoids to produce a metabolite that enhances interferon signaling.

“The metabolite is called desaminotyrosine, otherwise known as DAT,” Steed said. “When we gave DAT to mice and then infected them with influenza, the mice experienced far less lung damage than mice not treated with DAT.”

Next steps include identifying other gut microbes that may use flavonoids to influence the immune system, as well as exploring ways to boost the levels of those bacteria in people whose intestines aren’t adequately colonized with those microbes.

First of 10 expected BJC Investigators named

Helen McNeill, PhD, is the first researcher named as a BJC Investigator at the School of Medicine. The new BJC Investigators Program aims to recruit scientists who bring innovative approaches to major biological quandaries and whose discoveries stand to inform new ways of understanding disease and developing treatments.

McNeill, an international leader in the field of developmental biology, is a professor in the Institute of Medical Science and the Department of Molecular Genetics, both at the University of Toronto. She is also a senior investigator at the Lunenfeld-Tanenbaum Research Institute, part of the Sinai Health System in Toronto. Her appointment as a BJC Investigator and a professor of developmental biology begins Jan. 1.



COURTESY OF HELEN MCNEILL

Helen McNeill, PhD, is an international leader in the field of developmental biology.

“We sought candidates who had already indelibly changed their fields, whose discoveries will result in new and fundamental shifts in scientific thinking and whose laboratories will become a nidus for additional innovative work across Washington University,” said David H. Perlmutter, MD, executive vice chancellor for medical affairs and dean of the School of Medicine.

The program is designed to specifically focus on basic science and is inspired by the Howard Hughes Medical Institute’s philosophy of investing in people with exceptional creative talent. It plans to bring 10 renowned researchers to the School of Medicine and the life sciences ecosystem of St. Louis.

“This program represents another joint effort between BJC and Washington University to help keep the school’s biomedical research at the forefront of discovery,” said Steven H. Lipstein, CEO of BJC HealthCare.

McNeill’s work is focused on understanding the processes that govern how cells make contact and work together to form the broader architecture of whole tissues, both during development and adulthood. Her work — spanning studies of fruit flies, mice and human genetic data — has relevance for understanding birth defects, cancer and diseases of specific organs, such as the kidney and lungs.



VIRGINIA KELLY

OUTmed Supporting LGBTQ rights

To help LGBTQ faculty, staff and students develop networking relationships and find mentors, the Department of Medicine recently launched OUTmed. One of its first priorities was to create OUTlist, a visible listing of medical school faculty, staff, house staff and students who identify as members of the LGBTQ community, and an ALLYlist of those who support LGBTQ rights and equality. OUTmed is committed to bringing national best practices in LGBTQ health care to the medical school. Left, OUTmed supporters marched in the St. Louis PrideFest parade June 25.

Learn more at internalmedicinediversity.wustl.edu/outmed

Malaria drug protects fetuses from Zika infection

Treatment prevents virus from crossing placenta to infect fetus, mouse study shows

Studying pregnant mice, School of Medicine researchers have learned that the Zika virus infects the fetus by manipulating the body's normal barrier to infection. Moreover, they showed that a malaria drug can interfere with this process, protecting the fetus from viral infection.

"We found that the malaria drug hydroxychloroquine effectively blocks viral transmission to the fetus," said senior author Indira Mysorekar, PhD, an associate professor of obstetrics and gynecology and of pathology and immunology. "This drug already is used in pregnant women to treat malaria, and we suggest that it warrants evaluation in primates and women to diminish the risks of Zika infection and disease in developing fetuses."

The findings are published in *The Journal of Experimental Medicine*.

To protect the developing fetus from infection, the body mobilizes robust defenses that keep microbes from ever reaching the fetus in the first place.

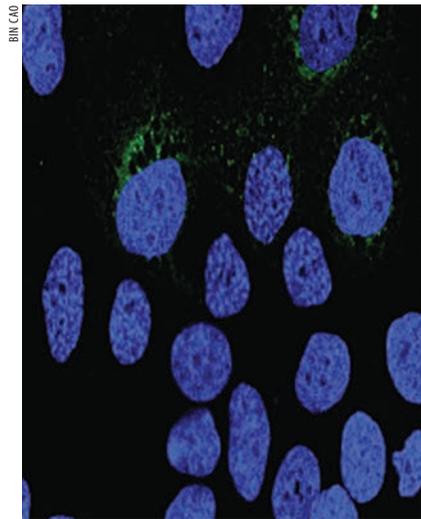
Mysorekar and others have shown that autophagy — the cellular waste-disposal pathway by which cells grind up debris, unwanted organelles and invading microbes — is an important part of the formidable placental barrier to infection.

Zika, however, not only can invade the placenta, but it can multiply there, Mysorekar and others have found.

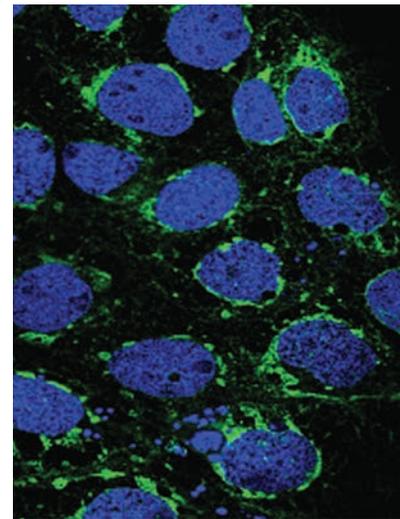
To understand how Zika breaches the placenta, Mysorekar, postdoctoral fellow Bin Cao, PhD, and colleagues infected human placental cells with the virus. Exposure to the virus activated genes related to autophagy, they found.

However, when the researchers treated the cells with drugs to ramp up the autophagy pathway, the number of Zika-infected cells increased. Drugs that suppressed autophagy resulted in fewer placental cells infected with Zika virus. In other words, the virus spread more effectively when the researchers dialed up the barrier response, and performed more sluggishly when they dialed it down.

Since hydroxychloroquine suppresses the autophagy response, the researchers questioned whether it also could protect fetuses against Zika. The researchers dosed



BIN CAO



Left: The malaria drug chloroquine — a close relative of hydroxychloroquine — prevents the Zika virus (green) from growing in human placental cells (blue). Right: The drug rapamycin prompted the virus to grow rapidly.

Zika-infected pregnant mice with either hydroxychloroquine or a placebo. They found significantly less virus in the fetuses and placentas from the mice that had received hydroxychloroquine. In addition, these placentas showed less damage and the fetuses regained normal growth.



HOWARD HUGHES FELLOWS Medical students Rukayat Taiwo (left) and Connor Liu have been selected to receive a year of mentored training with top biomedical scientists through the Howard Hughes Medical Institute's Medical Research Fellows Program. Taiwo is one of seven fellows to receive funding for a second year. She is analyzing glioblastoma on a molecular level with mentors Albert H. Kim, MD, PhD, and Joshua B. Rubin, MD, PhD. Liu is working with mentor Gavin P. Dunn, MD, PhD, to test computational strategies that may be used to design therapeutic cancer vaccines.

Dean emeritus to lead University of Hawaii faculty practice



Larry J. Shapiro, MD

Larry J. Shapiro, MD, dean emeritus of the School of Medicine, is the new chief executive officer of University Health Partners of Hawaii, the faculty practice at the University of Hawaii John A. Burns School of Medicine.

A pediatrician, genetics researcher and mentor, Shapiro served as executive vice chancellor

for medical affairs and dean of the School of Medicine from 2003 to 2015. "Serving Washington University School of Medicine has been an enormous privilege," Shapiro said. "It is a remarkable place, with many amazing and talented individuals who work, study and teach here. I have been associated with Washington University for more than 50 years as a student, a parent and a faculty member. I owe an enormous debt to the many people that have meant so much to me during that span of time."

Shapiro said he plans to return to St. Louis often and represent the university in Japan for the McDonnell International Scholars Academy.

Medical education leader appointed

Eva Aagaard, MD, formerly a professor of medicine and associate dean for educational strategy at the University of Colorado School of Medicine, has been named senior associate dean for education.

"Eva is a visionary with a glowing reputation nationally and internationally for her leadership and innovation in medical education," said David H. Perlmutter, MD, executive vice chancellor for medical affairs and dean of the School of Medicine.

Aagaard succeeds Alison J. Whelan, MD, who joined the Association of American

Medical Colleges (AAMC) as its new chief medical education officer. Mary E. Klingensmith, MD, the Mary Culver Distinguished Professor of Surgery and vice chair for education in the Department of Surgery, served as senior associate dean for education in the interim.

At the University of Colorado, Aagaard founded the Academy of Medical Educators, which works to promote teaching excellence through faculty certificate programs in medical education and leadership, one-on-one coaching, a longitudinal and online curriculum for faculty development and a residents-as-teachers program, among other initiatives. Aagaard also directed the Center for Advancing Professional Excellence, a standardized patient and simulation center.

Aagaard has served in national leadership positions with the American Board of Internal Medicine, National Board of Medical Examiners and the Society of General Internal Medicine. In those roles, she has collaborated with the AAMC and the Accreditation Council for Graduate Medical Education. A noted mentor for women in medicine, Aagaard works with dozens of committees and programs nationally and at the university level. "Mentoring women is important because they often lack access to mentors," she said. "Having a trusted colleague to help pinpoint priorities and identify ways to achieve goals can help them overcome unique challenges."

She and her husband, Russ Aagaard, a small-business owner, have two children.



Eva Aagaard, MD



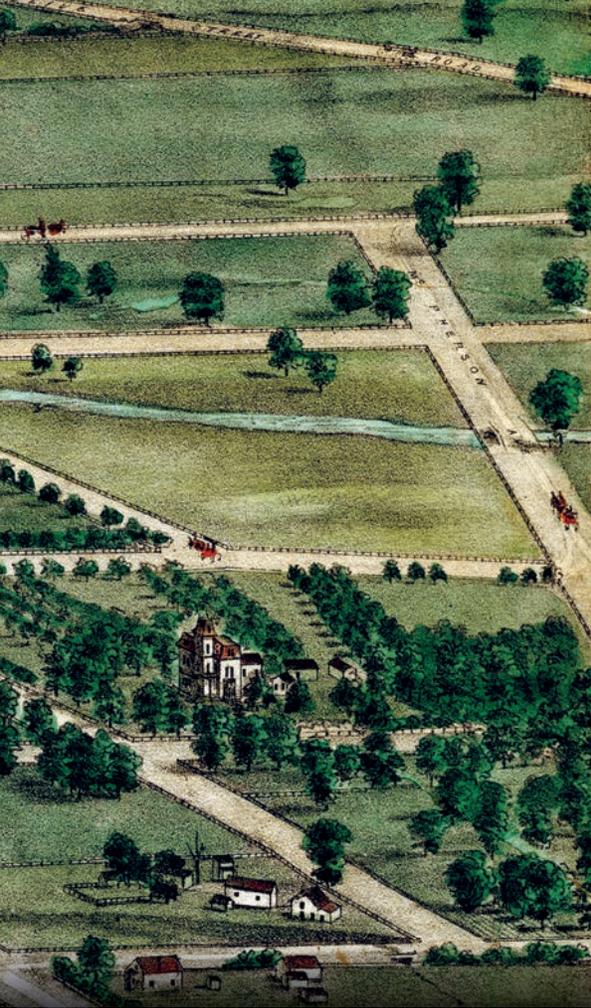
EXPLORE ST. LOUIS

Anchor

How medical center visionaries helped save the Central West End



Top: Over a century old, the Central West End, which abuts Washington University Medical Campus, is full of charming cafés, galleries, antique shops, restaurants and boutiques. A new book outlines the neighborhood's origins, period of affluence, decline and revitalization. Bottom: Delmar Boulevard and Taylor Avenue in 1916.



WELLS FARGO

What was the Central West End like before the School of Medicine was built?

By the time the new Washington University School of Medicine campus was dedicated in 1915, the Central West End (CWE) was by far the most desirable neighborhood in St. Louis. In 1875, when Compton and Dry created their famous bird's-eye views of the city, the CWE had been a sleepy, rural place, mostly farmland. But in the run-up to the 1904 World's Fair, and in the booming years afterward, that changed dramatically. High-end builders developed beautiful streets, including private places, along with chic commercial districts. Robert Brookings, the university board chairman who moved the medical school from downtown St. Louis to Kingshighway, bought a home for himself on Lindell, across from Forest Park. Religious congregations moved in, as did other hospitals. Many of the city's elite settled in CWE houses, including such noted School of Medicine physicians as Washington Fischel, George Gellhorn, W. McKim Marriott, Evarts Graham and Vilray Blair. A 1912 book, published by a local newspaper, listed the 4,000 most famous men in St. Louis — and most of them lived in the CWE.

As the medical school and its affiliate hospitals grew and prospered, what was happening in the neighborhood around it?

During the teens, 1920s and into the 1930s, the CWE flourished. Prominent people, such as David Francis — who was chief World's Fair organizer, St. Louis mayor, Missouri governor and ambassador to Russia — lived in giant houses, staffed by uniformed servants. At Kingshighway and Lindell, the William Bixby family owned the entire block and lived in a palatial home that later was demolished to make way for the elegant Chase and Park Plaza hotels.

When and why did the downturn in the neighborhood begin?

In 1927, a powerful tornado devastated parts of the CWE, killing 78 people and injuring 500. On many days, a pall of smoke, caused by coal fires and industrial pollution, hung over the area, and some residents began to look toward new suburbs with cleaner air. During the 1930s-era Depression, some of the large homes became unaffordable. Then at the end of World War II, the crush of returning soldiers created a huge demand for housing. Suddenly, owners had a great incentive to break up these large homes into rooming houses. In the 1950s and 1960s, some mansions were torn down for modern high-rises or even parking lots.

What was the Central West End's low point?

By the 1960s and early 1970s, the situation in the CWE had become critical. As Dr. Ron Evens (former head, Mallinckrodt Institute of Radiology, and former president, Barnes-Jewish Hospital) said: "People don't realize when you go to the CWE now, what it was like then. It was seedy. It was dirty. It was high crime. It was prostitutes. It was people drunk on the streets. So the issue became, 'Oh, my God, what are we going to do about that?'" Dr. Will Ross (nephrologist and associate dean) said that when he was here for a medical school interview, he was walking down Kingshighway when a policeman *behind* him began shooting at a man *in front* of him. In 1962, the medical center institutions banded together, forming the organization later called the Washington University Medical Center. Still crime was a serious problem for employees, who were being robbed on the streets. Other hospitals — St. John's, Shriners, Missouri Baptist and St. Luke's — started moving out of the area.

What did Washington University Medical Center do about it?

During the 1960s, Dr. William Danforth, then vice chancellor for medical affairs, began to worry about the flight of these hospitals and the fancy new “Palaces on Ballas” they were building in the western suburbs. He tapped the talented young Dr. Evens to head a committee that would consider three options: move the medical center west, stay put, or remain in place but build a clinical presence in the Plaza Frontenac area. Raymond Wittcoff (developer and Jewish Hospital board member) was a major advocate for staying in the city, and ultimately that view prevailed. Next Wittcoff contacted an architectural firm to design a plan for the Central West End. But the proposal called for razing a huge swath of the area — and somehow it was leaked to a local newspaper. People living in the neighborhood, who were working hard to save it, were horrified.

“That decision (to stay) may be one of the five most important decisions ever made in terms of the history of the city of St. Louis. Because if the Washington University Medical Center had left ... can you imagine what the city of St. Louis would be like?” — Jerry King

What did the medical center try next?

They needed a new approach. So Dr. Danforth, who became university chancellor in 1971, had lunch with developer Richard Roloff, then working for Capitol Land Company, and he generously agreed to take on volunteer leadership of a new revitalization effort. He did a spectacular job, though it was tough going. At his first meeting with residents, he encountered a crowd still angry from the newspaper article. As he recalled, every one of those people would cheerfully have bought him a one-way ticket to California! But he persisted, hiring urban design firm Team Four to devise a plan that would save as much historic architecture as possible, acquire homes from residents ready to leave and re-sell them to

young buyers, eager to renovate. He and his team also brought in a major client, Blue Cross, to new headquarters that later became the 4444 building on Forest Park Avenue.

How successful was this revitalization effort?

It was extraordinarily successful. The Washington University Medical Center Redevelopment Corporation (WUMCRC) — headed successively by executive directors Jerry King, Eugene Kilgen and others — worked in partnership with area residents and the medical center, particularly psychiatrist Dr. Samuel Guze, who succeeded Dr. Danforth as vice chancellor for medical affairs. They bought up dilapidated homes, such as those on the 4300 and 4400 blocks of Laclede; often the elderly owners would greet them at the door and say gratefully, “Where do I sign?” Then they attracted young families — even the new superintendent of the St. Louis schools — to buy and rehab them. A diverse group of people moved in. They also encouraged new businesses to come in. Of course, the medical school and the hospitals have since thrived and grown substantially, with more than 20,000 people working there daily. One surprise has been that the WUMCRC, initially viewed as a decade-long effort, continues today under executive director Brian Phillips. The CWE now is a vibrant mix of historic buildings and new development.

How does the future look for the Central West End and surrounding neighborhoods?

The future of the CWE is very bright, and its success also has been a catalyst for growth in other neighborhoods. The Forest Park Southeast area, now known as The Grove, began a major renewal under the leadership of William Peck, then dean of the medical school, and Dr. Jerry Flance, who worked with residents and urban pioneers. And the new Cortex Innovation Community, a 200-acre technology district to the east, developed there in part because startup businesses liked the proximity to the medical center and to the diverse, exciting CWE. Today, Cortex is one of the fastest growing technology startup scenes in the U.S., with more than 250 companies on site. So the WUMCRC’s valiant efforts in the 1970s and beyond have certainly had a wide-reaching impact. □



Art gallery in William Bixby's palatial home, c. 1904



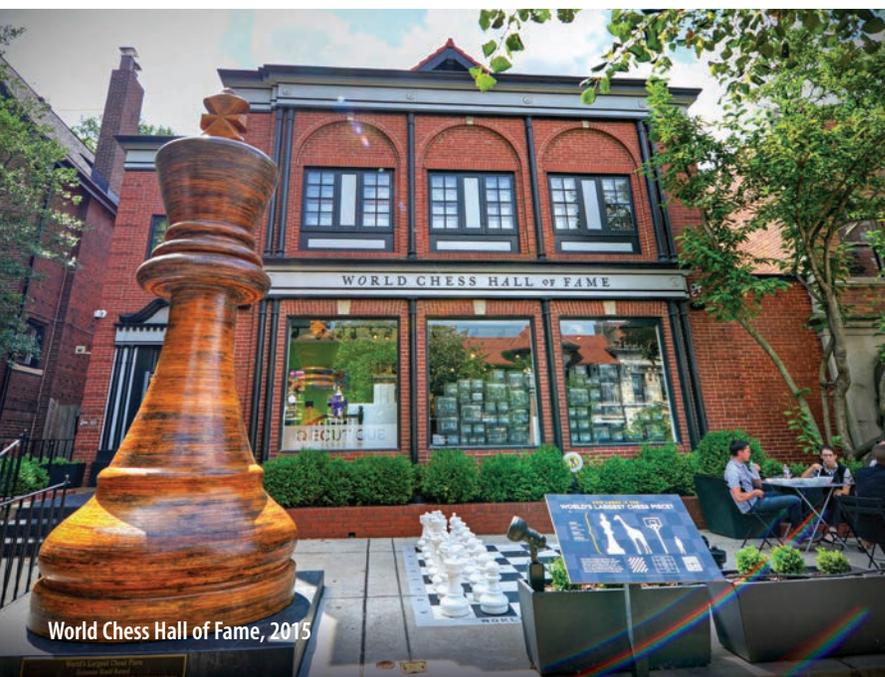
Dilapidated buildings with Grand Avenue skyline in background, 1961



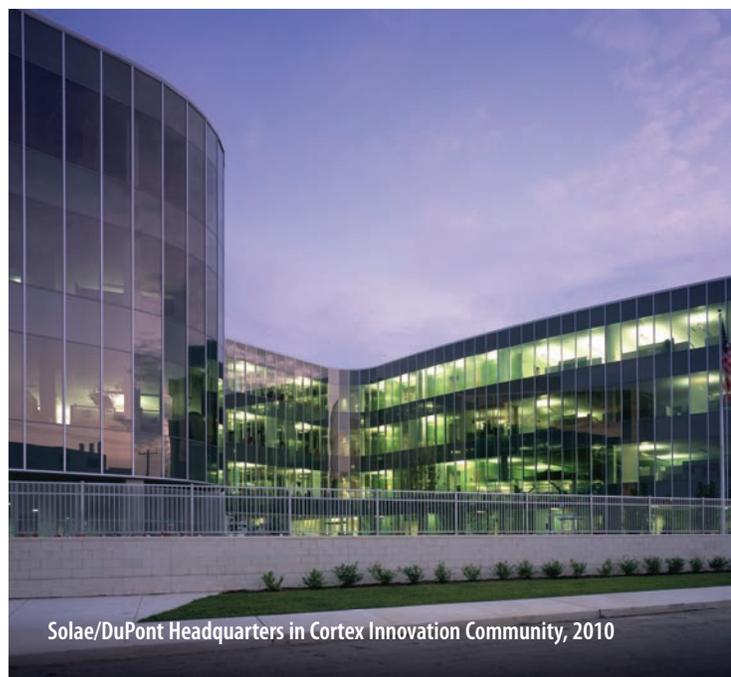
Dr. Carl Moore lectures in Barnes Amphitheater, 1943



Dining today in the Central West End



World Chess Hall of Fame, 2015



Solae/DuPont Headquarters in Cortex Innovation Community, 2010



Inside an epidemic

Overcoming America's opioid crisis starts with understanding abuse patterns

BY GAIA REMEROWSKI

Theodore Cicero's research changed direction when he encountered a 20-year-old who was taking opioids — but not to get high.

The young man was struggling with depression, low self-esteem and social anxiety. He was taking drugs because he believed they made him a better, more popular person. He was more social, more relaxed and was able to approach women in bars and start conversations. And he was taking opioids despite the disastrous consequences he knew they could have.

Cicero, PhD, the John P. Feighner Professor of Psychiatry, has surveyed 25,000 addicts on why they use drugs. It's stories like the young man's that illuminate the challenge medical professionals face in fighting drug use.



“**T**he typical survey response is not that they are getting high, but that it relieves their depression, they feel less anxious,” Cicero said. “Many people feel they are actually better individuals when they’re taking drugs because they are more outgoing. People think they function better. That’s a difficult thing to combat.”

This is the power opioids, such as the prescription pain pill oxycodone or the more easily obtained illegal heroin, have on many individuals and is one major reason the drugs are so addictive. In 2014, drug overdoses surpassed automobile accidents as the No. 1 cause of accidental death for the first time in U.S. history. And although not all of these overdoses are due to opioids, 91 Americans die every day from an opioid overdose, according to the Centers for Disease Control and Prevention (CDC). CDC data also show that 60 percent of overdoses occur in patients with legitimate prescriptions from a single doctor.

For 25 years, Cicero has been ahead of this developing crisis, charting addicts’ motivations and predicting emerging abuse patterns around the country. Cicero and colleagues were the first to identify changing demographics as opioid addiction spread from inner cities to the suburbs, and also predicted the shift from painkillers to heroin to synthetic opioids like fentanyl.

For more than 25 years, psychiatrist Theodore Cicero, PhD, has been on the leading edge of the opioid epidemic, surveying some 25,000 addicts around the country.

How did we get here?

“There are two events that happened in the late ’90s and early 2000s that have led to where we are right now,” Cicero said.

In 2001, the Joint Commission accrediting organization, advocating on behalf of patients, issued a set of standards outlining how the health-care industry was vastly undertreating pain. The report recommended that health-care workers consider pain as the “fifth vital sign,” along with monitoring of a patient’s temperature, pulse, respiration and blood pressure.

As a result, health-care workers routinely began asking patients to rate their pain on a pain scale. The overarching message: patients shouldn’t have to endure pain.

The report also urged physicians to prescribe opioids more freely, based on a letter published in 1980 in *The New England Journal of Medicine* (NEJM). Written by two doctors, the five-sentence letter stated: “We conclude that despite widespread use of narcotic drugs in hospitals, the development of addiction is rare in medical patients with no history of addiction.” Though the letter since has been debunked, drug makers and doctors still cite it as a reason to continue the widespread prescribing of opioids.

Another event that took abuse to a critical level was the 1996 introduction of an extended-release version of oxycodone, one of the most popular opioid painkillers.

Sold under the brand name OxyContin, the new pills could be taken just once or twice a day, rather than every 4 to 6 hours. “For people who had trouble keeping track of their medications, this was an ideal solution,” Cicero said. “Elderly people, for example, especially have memory issues with that.”

This new formulation, however, also was an ideal solution for addicts. For a pill to work over 24 hours, it must contain a large amount of the active drug. Instead of 5 mg, each tablet now contained 80 to 100 mg of oxycodone. Addicts soon learned they could release the drug’s full potency all at once by crushing the new tablets.

The revised formulation also contained no acetaminophen or non-steroidal anti-inflammatory drugs, both of which make snorting and injecting the drug very painful. (Acetaminophen, for instance, burns the nasal passages when snorted.)



JERRY NAUHEIM

From pain pills to heroin

How misunderstandings and good intentions drove the worst drug crisis in U.S. history

1980

MISINFORMATION

A now-debunked letter in The New England Journal of Medicine deems painkillers as rarely addictive.



PAIN SCALE

The Joint Commission suggests pain is vastly undertreated and urges doctors to consider it as the "fifth vital sign."



OPIATE EXPLOSION

Doctors prescribe larger amounts of opioids, which end up on the street. An extended-release version of OxyContin containing 10 times more active ingredient is developed, making it easier to crush and snort.

SUPPLY LIMITS

As doctors realize the abuse potential, they limit prescriptions, decreasing supply and increasing costs of opioids on the streets.



DETERRENCE EFFORTS

Drug company makes a version of OxyContin that is more difficult to crush and snort. This inadvertently drives addicts to heroin.



HEROIN

The epidemic increases over time. Addicts' demographics shift from poor, predominantly black communities to more white, middle- to upper-class communities.

TODAY

FENTANYL

Dealers realize cutting heroin with the far more potent, cheaper, lab-made opioids fentanyl and carfentanyl gives users a better — but often fatal — high.



?



David Tan, MD (standing), chief of the emergency medical services section, explains naloxone administration to Missouri park rangers at Babler Memorial State Park in Wildwood. Naloxone, or Narcan, is a nasal spray that works as an opioid antidote. Frontline responders, such as highway patrol officers, park rangers and conservation agents, now keep Narcan at their disposal.

“Now all of a sudden we had a pure version of oxycodone that didn’t contain any additives,” Cicero said. The maker of this extended formula and the Food and Drug Administration (FDA) later stated that they did not foresee addicts’ workarounds.

With a new emphasis on curing pain and the discovery of a more potent delivery method, other pharmaceutical companies began producing variations of these pain pills. Doctors became more willing to prescribe opioids in larger amounts. Many of these prescriptions would go unused, stored in medicine cabinets and end up getting stolen, sold and diverted to the streets. “Now you have a ready supply of it on the street because physicians were doing their job and treating pain, but had no indication that this was going to lead to trouble,” Cicero said.

Gathering abuse data

In the 1990s, Cicero worked on an FDA advisory committee evaluating the abuse potential of drugs undergoing approvals. Before long, a drug company sought his help in gaining federal approval for a new opioid named tramadol, or Ultram. To determine its abuse potential, Cicero suggested sending surveys to U.S. drug treatment centers for patients to confidentially complete.

Center directors would not read these surveys; instead, responses would go to Cicero’s research group at the School of Medicine. This helped legitimize the project and prompted addicts to be more forthcoming with their answers.

“Addicts felt the survey was for a good purpose and that we were trying to solve a problem that they had,” Cicero said. “They’re desperately looking for someone who will either help them with their treatment or maybe prevent this crisis in the first place.”

Over the past two decades, Cicero’s team has sent out confidential questionnaires to approximately 150 drug treatment centers nationally to better understand addiction. Most clients choose to remain anonymous, but some agree to be identified and even participate in lengthier interviews with Cicero.

Survey data is collected in real time. This enables the researchers to put their “ears to the ground,” identify new types of drug abuse and quickly inform regional first responders and agencies about impending threats.

“I don’t think there’s anyone that does a more thorough and accurate survey of drug abuse than Ted Cicero,” said John Burke, past president of the National Association of Drug Diversion Investigators and a retired Ohio police commander who served on the force more than 50 years. He now runs Pharmaceutical Diversion

Overdose antidote

Narcan is an antidote that rapidly reverses the effects of an opioid overdose; it has no adverse effects if administered to a person who is not overdosing. The drug is available at many pharmacies without a prescription.



1 Check for signs of an overdose

Signs include: lack of responsiveness, shallow breathing, pinpoint pupils, blue/gray lips or fingernails, clammy/pale face. Call 911.

2 Administer Narcan

If, based on these signs, you suspect an overdose, administer Narcan nasal spray in one nostril. The spray is absorbed through the blood vessels in the nasal membranes.

3 Monitor response

The drug then travels to the brain, where it replaces the opioid molecules that are bound to opioid receptors. Narcan works to revive victims in 2-5 minutes. If needed, administer second dose.

Education Inc., an organization that educates law enforcement and health professionals about the dangers of diversion (the illegal theft and sales of pharmaceutical drugs).

Cicero's studies helped verify opioid abuse trends in Ohio, a state hit particularly hard by this crisis. The findings "over and over are consistent with what we see on the street," Burke said, and have been a reliable source for educating the public about the changing face of opioid abuse.

Cicero and his colleagues also publish survey data and analyses in national scientific journals and keep the FDA abreast of their findings. While the agency collects its own data, the gathering process extends over much longer time periods and is often published years later.

A new drug of choice

When doctors realized the NEJM letter was wrong and that there actually was a very large abuse potential for painkillers, they began limiting the quantity of pills they prescribed. Purdue Pharma also switched to an abuse-deterrent formulation of OxyContin that was much more difficult to crush and snort. These changes kept some of the pills off the streets and slowed their abuse but had the unintended consequence of forcing addicts, who

were unlikely to stop using drugs altogether, to find a substitute. That substitute, for the most part, was heroin.

In 2014, Washington University was the first to signal this shift from prescription opioids to heroin, a cheap and easily accessible alternative. As more people used heroin, the less stigmatized it became. Suddenly heroin started showing up in affluent suburban neighborhoods and schools. Cicero's surveys uncovered these shifts in users' demographics: Half of those who began using heroin before 1980 were white, but over the past decade nearly 90 percent of those who began using were white.

The surveys also helped reveal the use of fentanyl, a synthetic opioid, which began to show up in much of the heroin responsible for overdoses, and carfentanyl, a derivative of fentanyl that is used to tranquilize elephants. Fentanyl and its derivatives are 50 to 100 times more potent than heroin, provide a more intense "high" for the user and are relatively inexpensive to make in the lab.

Knowing fentanyl and similar drugs were becoming a problem has helped federal authorities to better monitor availability and block importation of the drugs into the country. First responders also have learned to use caution as some of these drugs can be deadly — even in small amounts — if accidentally inhaled at the scene of an overdose.

Moving beyond fear

All of this misuse has had a chilling effect on doctors, who now may be resistant to prescribing opioids, even to those who need them. “Physicians are really at a disadvantage now not knowing who to treat and who not to treat,” Cicero said. “Given all the publicity surrounding this problem, and now the escalation to heroin, most physicians have gotten to the point where they’re afraid to prescribe these medications.”

Doctors must learn to ask questions about patients’ previous history of drug use, alcohol use and smoking, as well as any past anxiety or depression, Cicero said. These are all potential markers of abuse. Cicero also believes physicians need to be more cognizant about the amount of opioids they are prescribing: Is a 30-day supply really necessary in most cases?

“Physicians are really at a disadvantage now not knowing who to treat and who not to treat.” — Theodore Cicero, PhD

To help improve opioid prescribing practices, Cicero suggests that medical schools add opioid and alternative pain management, as well as addiction education, to the curriculum. Medical students graduating today generally are not equipped to deal with the crisis.

“Most physicians don’t really know how to effectively treat pain. We don’t teach them,” Cicero said. “They don’t know how to manage pain and they certainly don’t know the signs that a potential patient is going to be vulnerable or susceptible to abuse.”

Evan Schwarz, MD, assistant professor of emergency medicine, and his team are on the frontlines, treating at least two to three addicts a night in the Barnes-Jewish Hospital Emergency Department (ED). When possible, the team administers Suboxone, a medication that limits cravings, as part of a project funded by the Behavioral Health Network of Greater St. Louis.

General practitioners can undergo training to learn how to administer Suboxone and similar addiction treatment drugs, Schwarz said. This way, they can treat regular patients who show signs of opioid abuse on an outpatient basis, which could help relieve the strain on treatment centers.

Providing patients with realistic pain management expectations can go a long way in preventing addiction, Schwarz said. Zero pain may not be achievable and patients may need to endure some measure of pain in certain circumstances. When appropriate, physicians and patients should seek out alternative forms of pain control via pain management specialists, physical therapists, meditation and so forth. “We try to let patients understand that we’re going to do our best to control their pain and give them realistic expectations for what we can do,” he said. “And even if we’re prescribing opioids, we want to do it in a safe and limited way because these medications do have risks.”

Washington University emergency physicians David Tan, MD, and Jeffrey Siegler, MD, also are leading regional medical training for first responders on naloxone administration. Naloxone, or Narcan, works as an opioid antidote, reversing an overdose within seconds. Narcan has saved nearly 27,000 lives, according to the CDC.

The training is part of a federal grant from the Substance Abuse and Mental Health Services Administration, in partnership with the National Council on Alcoholism and Drug Abuse.

The program educates first responders about misconceptions surrounding opioids. “Some people, when they start the training, are sitting there with a scowl on their face, with their arms crossed,” said Tan, also chief of the emergency medical services section. “And they think that these heroin addicts can choose to stop like we choose to stop at a red light and go at a green light. And it’s just not that easy for many of these people.”

To help prevent repeat overdoses, something the responders see all too often, the training also emphasizes the importance of referring addicts to treatment centers, Tan said.

Even with treatment, though, it is not easy to recover from opioid addiction. “The average number of times our patients have been in treatment is 4.8, almost five times,” Cicero said. “And some people are sober for years and then slip back into it because that feeling that they get with this drug — how it makes them feel like a better person — is going to be with them forever.”

“The ability to understand this, to get qualitative data has turned out to be extremely important. And we’re now on the leading edge of being able to use these data methods to understand more about what motivates abuse and how to mitigate it.” □

Making the invisible visible

A large, detailed fluorescence microscopy image of a mouse kidney section. The image shows a complex, porous structure of cells and tissue. The cells are stained with two different dyes: one in red and one in blue. The red staining is concentrated in certain areas, particularly towards the edges of the kidney section, indicating oxygen starvation. The blue staining is more widespread, covering most of the kidney's surface. The overall appearance is that of a highly textured, three-dimensional structure.

Imaging center brings
the science of life to light

BY TAMARA BHANDARI

Cells near the edge of a mouse kidney glow red, a sign that they are starved for oxygen. This is an important clue for researchers studying how the kidney responds to injury. Image taken on Zeiss Axioscan Z1 Automated Slide Scanning System.

Twelve feet tall and weighing several tons, the microscope capable of generating the voltage of a stun gun looms over James Fitzpatrick, PhD, as he circles it, deftly opening latches and detaching panels. A door on the side swings open, revealing a tangle of wires and, near the top, a shelf the size of a tape cassette. When the machine is fully built and turned on, a robotic arm will reach down, pick up experimental samples placed on the shelf and insert them into a column deep inside. There, the samples will be bombarded with electrons.

And the invisible will be unveiled.

This instrument that Fitzpatrick has so painstakingly unsealed is a top-of-the-line cryo-electron microscope. It is capable of magnifying the living world's tiniest structures — bacteria, viruses and biomolecules — a million or more times, bringing the unimaginably small up to a human scale.



TIM PARKER

“It’s a complicated beastie,” said Fitzpatrick, grinning. He is director of the Washington University Center for Cellular Imaging, known as WUCCI and pronounced Wookiee.

He has spent the better part of the spring and summer overseeing the installation and calibration of the \$7.2 million microscope, and he will put it through weeks of testing before making it available to the center’s clients later this fall. The machine is the cornerstone of a significant investment in cellular imaging. Advances in the field are transforming biomedical research, and WUCCI is keeping Washington University at the forefront.

Introducing the WUCCI

WUCCI sprawls across 6,000 square feet in the basement of the McKinley Research Building (to be renamed the Debra and George W. Couch III Biomedical Research Building) on the Medical Campus. It houses 15 of the most advanced microscopes, as well as banks of high-powered computers that are needed to analyze the mountains of data they produce.

The scopes can take 3-D images of viruses, make movies of living neurons as they signal one another, visualize the beating hearts of small animals such as worms and fish and map the structure of proteins down to the location of each atom.

Since the center’s establishment in 2015, researchers have imaged everything from living zebrafish and butterfly eyes to plastic catheters and rocks.

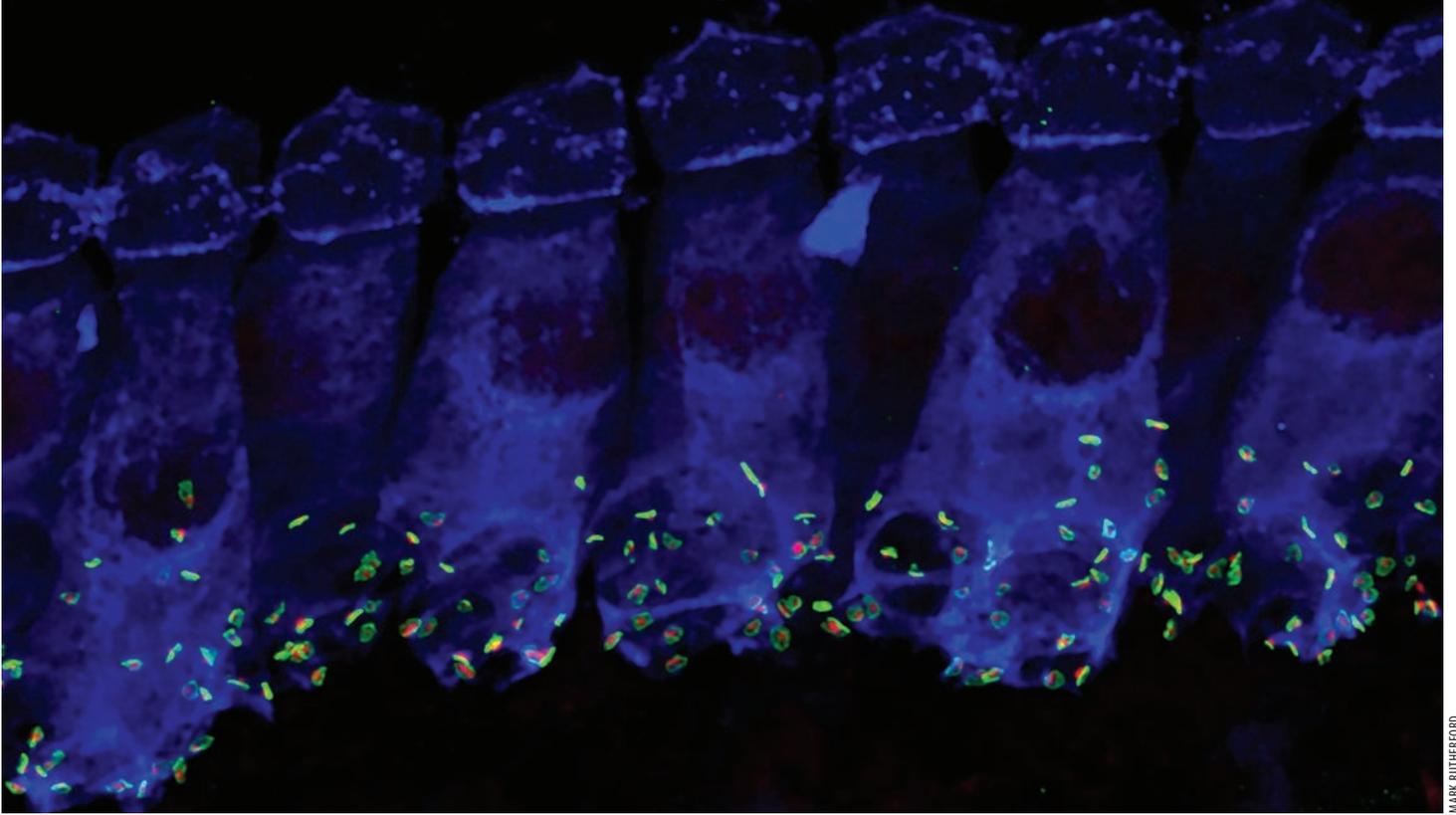
Today, more than 500 Washington University researchers representing some 220 labs use the center, and Fitzpatrick is hoping to draw more.

Cornerstone of biology

When Anton van Leeuwenhoek looked through the first microscope more than 300 years ago and saw legions of previously unimagined life forms wriggling underneath, he established one of the foundations of modern biology.

“Imaging is one of the cornerstones of biology and biomedical science,” said Azad Bonni, MD,

James Fitzpatrick, PhD, adjusts the wiring inside the center’s new cryo-electron microscope. The instrument visualizes objects as small as a few billionths of a meter, allowing researchers to map the location of each atom in a protein.



MARK RUTHEFORD

PhD, the Edison Professor and chair of the Department of Neuroscience. “Whatever questions we’re trying to answer, it all comes down to cells, because they are the fundamental unit of living things.”

Modern research microscopes are as far from Leeuwenhoek’s single-mounted lens as smart phones are from Alexander Graham Bell’s invention. They not only take snapshots of cells mounted on slides, they can record movies of a fertilized egg developing into an embryo, or of an immune cell chasing a bacterium. They can focus deep inside bones, tumors and even small animals, allowing scientists to see cells and tissues in their natural environment. They reveal our DNA. Microscopy makes the invisible visible.

WUCCI builds on the strengths of the departments of Neuroscience and of Cell Biology and Physiology, which operated separate imaging facilities for a number of decades. About five years ago, at funding renewal time, department leaders questioned whether to re-establish separate facilities or join together. “It occurred to us that it might be a good idea to create a collaborative center greater than the sum of its parts,” Bonni said.

The neuroscience imaging facility specialized in light microscopy, which allows researchers to attach fluorescent markers to specific molecules or cells, color-coding their images. Such technology suits researchers who often study how cells respond to cues, and circuits of cells and the synapses connecting them.

Cell biologists lean more heavily on electron microscopy, which images objects tens to thousands of times smaller than cells. Electron microscopes reveal precisely how the essential molecular machinery of the cell operates and how molecules involved in disease might be targeted with drugs.

Members of both departments — Paul Taghert, PhD, and Bonni from Neuroscience, and Helen Piwnicka-Worms, PhD, Robert Mecham, PhD, David Piston, PhD, and Phyllis Hanson, MD, PhD, of Cell Biology and Physiology — advocated for this core center and engaged in discussions across the medical school. Taghert and Hanson traveled the country, gathering the best ideas from leading imaging facilities. Ultimately, Fitzpatrick was recruited from The Salk Institute in San Diego. “We sold him on the idea that he could build something big here,” Bonni said.

Institutional resource

Modern imaging is key to understanding and treating many diseases. Thirty years ago, there were no microscopes that could map the blood vessels inside a solid tumor, or trace the outlines of each molecule in a virus’s shell. That technology now hums and clicks and reshapes medicine in Fitzpatrick’s center, and researchers increasingly rely on it. With every technological improvement, microscopy has grown more central to biological research ... and more expensive.

To study how sound is transmitted from the ear to the brain, researchers stained specialized sound-detecting cells (blue) and their synapses (red/green) in a mouse inner ear. Image taken on Zeiss LSM 880 Airyscan Microscope.

Imaging life

Modern microscopes can image objects ranging in size from insects to molecules.

X-RAY MICROSCOPY

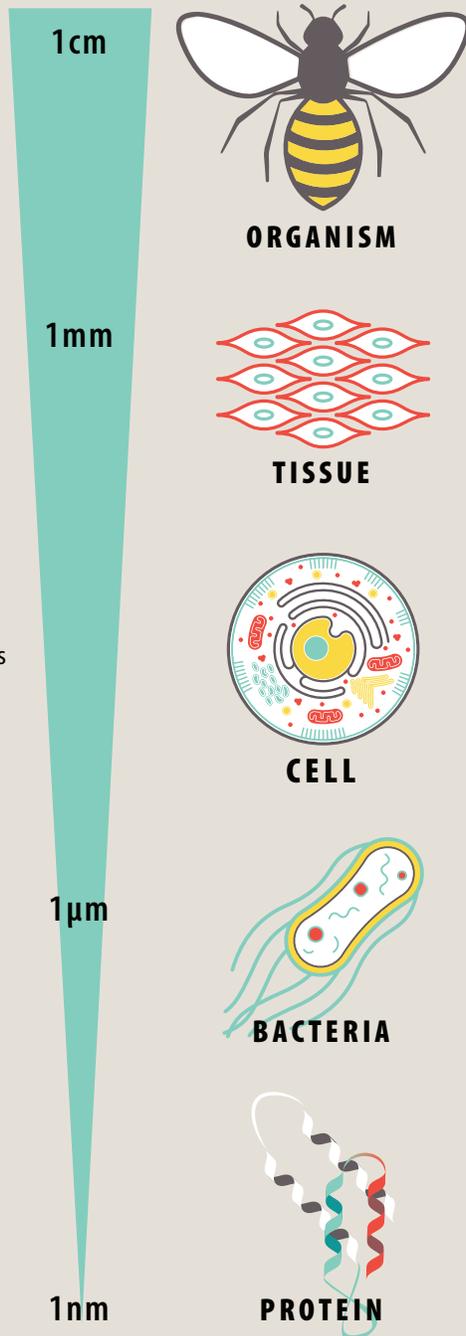
X-rays can penetrate deep into the body to image internal organs, tissues and whole small animals such as worms and insects.

LIGHT MICROSCOPY

The oldest form of imaging, light microscopy illuminates tissues, cells and some bacteria. Molecular labels that fluoresce in every color of the rainbow allow researchers to color-code their images.

ELECTRON MICROSCOPY

Electron microscopes use a concentrated beam of electrons to visualize the very smallest objects – bacteria, viruses, molecules, even atoms.



UNIT OF MEASUREMENT

1 cm = 1 centimeter = 1/100 of a meter

1 mm = 1 millimeter = 1/1,000 of a meter

1 μm = 1 micrometer = 1/1,000,000 (millionth) of a meter

1 nm = 1 nanometer = 1/1,000,000,000 (billionth) of a meter

“Many researchers need access to a wide range of imaging tools but could never afford to have them in their lab,” said Piston, the Edward Mallinckrodt Jr. Professor and head of Cell Biology and Physiology. “Often that means that young investigators have to make compromises on their choice of projects, but having access to WUCCI allows them to think more broadly.”

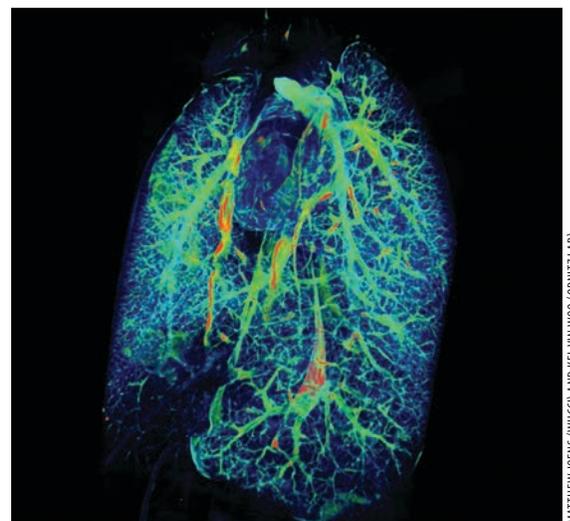
Furthermore, effectively using the high-tech equipment requires skills that can be difficult for small research groups to obtain.

“As the technology becomes more complicated, it takes more and more specialized expertise to get the most out of it,” Piston said. “In a large central facility, we can afford to hire and train the right specialists.”

Fitzpatrick likes to call the facility a one-stop shop, because the seven full-time staff members — all scientists themselves — are prepared to help with any stage of research.

“I have sat down with people at WUCCI and talked about basic cell biology,” said Clifford Luke, PhD, an associate professor of pediatrics who has used the center’s super-resolution light microscopes. “If you tell them what question you’re trying to answer, they will help you figure out the best way to do the experiment and which microscope is best suited for it.”

WUCCI has a suite devoted to sample preparation, containing equipment such as diamond knives sharp enough to cut extremely thin slices of tissue. Just as sets for TV shows



X-ray tomography detects an emulsion of gold nanoparticles, tracing the network of blood vessels in a mouse’s lungs and heart. Image taken on Zeiss Versa 520 X-Ray Microscope.

MATTHEW JOENS (WUCCI) AND KELVIN WOO (ORNITZ LAB)

became more realistic as high-definition TVs became commonplace, sample prep has become more important — and more elaborate — as microscopy has improved.

“When the resolution wasn’t as good, the quality of the sample prep didn’t matter as much,” Fitzpatrick said. “If something was a bit distorted, you couldn’t tell. These days, the quality of sample prep is of paramount importance.”

Immense computing power is required to process the complex datasets that come off the microscopes. Powerful computers line one wall of the center, and center staff can assist with analysis.

Pushing the limits

WUCCI is the latest step in a long history of imaging strength and innovation at Washington University. The first electron microscope built in the U.S. was designed and constructed by Gordon H. Scott, PhD, associate professor of cytology in the Department of Anatomy, around 1935.

More recently, Timothy Holy, PhD, the Alan A. and Edith L. Wolff Professor of Neuroscience, developed a form of light-sheet microscopy, which allows scientists to view thousands of cells at a time. Holy used this variation on the technique to scan more than 10,000 cells in a mouse’s nose to find the rare ones that turn on when the animal sniffs a particular pheromone.

Now, WUCCI staff are pushing the next frontier of imaging: virtual reality.

“We have microscopes that produce these beautiful, detailed 3-D images, but then we display them on a flat 2-D screen,” Fitzpatrick said. “We think that if people can take their results, hold them in their hands, turn them around, and look at them from all angles it will generate new ideas and understanding.”

Michael Shih, PhD, a center research specialist, has begun developing software that can convert researchers’ 3-D images into a virtual reality. The goal is to create an immersive environment to navigate biological samples ranging in scale from molecules to organ systems.

Although a virtual still image allows researchers to manipulate and inspect a virtual object, a virtual reality movie would allow people to watch from the inside as a biological process took place. Imagine standing at a cell’s midline and watching as the chromosomes lined up around you and then pulled apart into two daughter cells.



TIM PARKER

“Hardly anyone is working on the applications of virtual reality in microscopy,” Fitzpatrick said. “This is something we are working on offering that no other imaging facility can do.”

Wearing a headset and hand controllers, Michael Shih, PhD, explores the virtual reality scene he has created from a researcher’s 3-D still image.

Looking ahead

WUCCI has the potential to transform how biology is done at Washington University. The center ranks among the top five best in the U.S., as measured by the quality of the microscopes and the power of the computers. Staying in that position requires an ongoing commitment. Increasingly, other departments are contributing specialized equipment. The cryo-electron microscope, for instance, was jointly purchased by the offices of the provost and the medical school dean and other medical school departments led by Biochemistry & Molecular Biophysics and Cell Biology & Physiology.

“More and more, biomedical research depends on new technology,” Piston said. “There has been a lot of expertise in imaging at Washington University for a long time, but it has been distributed in different departments and centers, and it was difficult for researchers to find all the parts they might need, or to even learn that those were available. “With WUCCI, we now have the ability to access the newest technology through shared contributions.” □

Advancing human health

Edison Family Fund supports gut microbiome research

BY MARY LEE

The advent of genomic medicine has created the need for a new type of scientist — one able to translate genetic data into clinically relevant research that improves human health.

For nearly 15 years, the interdisciplinary Center for Genome Sciences & Systems Biology at the School of Medicine has provided a fertile proving ground for this new breed of investigator.



Jeffrey Gordon, MD, studies the microbial communities that colonize the human gut. His work has revolutionized understanding of how gut microbes shape human health and disease. Talented students and postdoctoral researchers such as Carrie Cowardin, PhD (left), and Vanderlene Kung, MD, PhD, assist him.

Working at the interface of computational and experimental biology, the center's faculty members and students have developed novel approaches to address some of the world's greatest health challenges, including obesity, childhood malnutrition and antibiotic resistance.

To help advance the center's innovative research and training programs, a St. Louis family with a long history of investing in the School of Medicine has contributed \$10 million to Washington University. This gift from the Edison family through the Harry Edison Foundation will create the Edison Family Fund to support the Center for Genome Sciences & Systems Biology and the work of its director, Jeffrey Gordon, MD, the Dr. Robert J. Glaser Distinguished University Professor. In recognition, the center is being named the Edison Family Center for Genome Sciences & Systems Biology.

"This gift will serve as an important catalyst for the School of Medicine's personalized medicine initiative," said Chancellor Mark S. Wrighton. "It will enhance our efforts to understand how our genetic differences influence our well-being and disease risk and empower a new generation of scientists to combat illnesses that affect millions."

The Harry Edison Foundation's first gift to the School of Medicine, made in 1967, established a professorship in surgery as a tribute to the foundation's namesake. Harry Edison, one of five brothers who founded a chain of shoe stores that became the fashion conglomerate Edison Brothers Stores, was a noted philanthropist and civic leader.

"For 50 years, the Edison family has been committed to supporting St. Louis' greatest institutions, including Washington University and its School of Medicine," said Andrew Newman, Harry Edison's great-nephew, a trustee of the Harry Edison Foundation and a longtime member of the university's Board of Trustees and member of the School of Medicine National Council. "We are excited to play a role in advancing the important work being done at the Center for Genome Sciences & Systems Biology. I have known Jeff Gordon for many years, and I have great confidence in his leadership and research."

Groundbreaking research

Gordon is internationally recognized for his pioneering role in establishing a field of research devoted to the human microbiome. His work focuses on the trillions of microbes that live in the gut, where they process foods and synthesize vitamins and nutrients that human cells can't manage on their own. Groundbreaking studies by Gordon and his trainees have linked these microbes and their genes to disease and good health.

After initially identifying the relationship between dysfunctional gut microbiomes and obesity more than a decade ago, Gordon and his students expanded their research to address childhood malnutrition, the leading cause of death worldwide in children under the age of 5. They have formulated new types of food-based therapies that are designed to repair the gut microbiota in malnourished children. Working with collaborators in Bangladesh, they are beginning to test the effectiveness of these therapeutic foods.

"This gift from the Edison Foundation will enable us to make strategic investments that allow our research community to evolve and remain vibrant," Gordon said. "I think it is a wonderful expression of trust on the part of the Edison family. Their belief in our center and our capacity to improve the health and well-being of people around the world encourages us to keep moving forward, especially in a time of uncertainty regarding federal funding for research."

Family's legacy

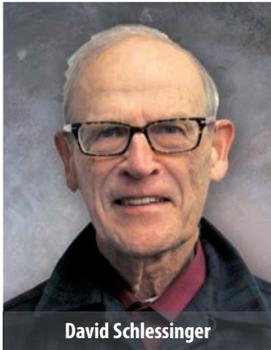
Previous gifts from the Harry Edison Foundation have supported a variety of initiatives and programs at the School of Medicine, including diabetes research, stem cell and developmental biology research, and the construction of the Eric P. Newman Education Center, named in honor of Andrew Newman's father, a 1935 graduate of Washington University's School of Law. The foundation also established a second professorship — the Edison Professorship in Neurobiology — in 1977.

Members of the Edison family have provided significant personal support and leadership across the university for many years.

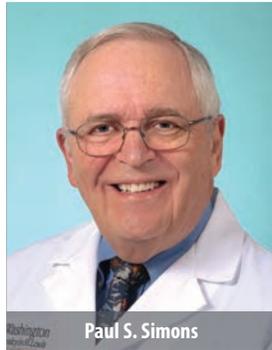


Harry Edison

EDISON FOUNDATION



David Schlessinger



Paul S. Simons



Col. Thomas R. Bürklow



J. William Campbell



Gary A. Ratkin

Alumni Association awards

Each year, the Washington University Medical Center Alumni Association honors a select group of graduates, faculty members, former residents and fellows for their professional achievements, community service and dedication to the university. Here are the 2017 recipients:

To read more about the recipients, go to wumcnews.org/2017awards

■ David Schlessinger, PhD

Distinguished Service Award

Schlessinger is a National Institutes of Health (NIH) Distinguished Investigator at the Laboratory of Genetics at the National Institute on Aging (NIA). He is internationally recognized for his pioneering work in basic molecular biology, including the mechanism of action of antibiotics and the application of human genetics and genomics to better understand disease.

In 1960, Schlessinger earned a doctoral degree from Harvard University, where he worked for DNA co-discoverer and Nobel laureate James Watson. Following two years of postdoctoral training at the Pasteur Institute, Schlessinger joined Washington University, where he served as professor of molecular microbiology, of genetics and of microbiology until 1997.

Schlessinger firmly established the study of human genetics at Washington University and is credited with positioning the school at the forefront of genetics research before he later moved to the NIA.

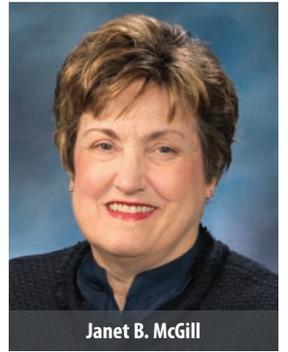
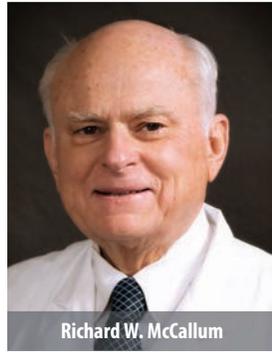
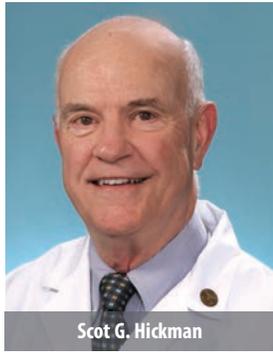
■ Paul S. Simons, MD '67

Distinguished Service Award

Simons, associate professor of pediatrics, is known throughout the pediatric community for his tireless dedication to the treatment of children and adolescents with developmental and behavioral disabilities.

Long before autism and attention deficit disorder (ADD) were in the national spotlight, Simons not only was identifying and treating children with these disabilities, he also was training numerous medical students and residents in developmental and behavioral pediatrics.

A devoted advocate of his patients, Simons also championed research, contributing heavily to the enrollment of clinical research subjects into research protocols at Washington University. The field of pediatrics has benefited greatly from the school's psychiatric studies of depression, autism, bipolar disease and ADD.



■ **Thomas R. Burklow, MD '87**

Alumni Achievement Award

Burklow, director for Population Health and HEDIS Compliance at Walter Reed National Military Medical Center, was recognized for 30 years of outstanding service as a clinical, academic and administrative leader in the nation's flagship military centers.

■ **J. William Campbell, MD '77, HS '80**

Alumni Achievement Award

Campbell is medical director for St. Luke's Medical Group and professor of clinical medicine at the School of Medicine. Among the earliest physicians in St. Louis to treat patients with HIV/AIDS, Campbell helped establish the medical school as a leading center for care of HIV-infected patients.

■ **Gary A. Ratkin, MD '67, HS '72**

Alumni Achievement Award

Ratkin, an associate professor of clinical medicine, is a distinguished oncologist, medical ethicist and palliative care physician. His ideas regarding living longer and better through palliative care have served as the basis for teaching how to care for chronically ill patients.

■ **Charles W. M. Roberts, MD/PhD '95**

Alumni Achievement Award

Roberts is director of the Comprehensive Cancer Center and executive vice president at St. Jude Children's Research Hospital in Memphis. An international expert in cancer epigenetics and a dedicated pediatric oncologist, colleagues regard him as an accomplished leader who moves seamlessly from research to clinical care.

■ **Scot G. Hickman, MD '70, HS '77**

Faculty Achievement Award

Hickman, a professor of medicine, is renowned for outstanding mentorship of medical students, residents and junior faculty. He has taught the hematology section of the medical school curriculum for 30 years and the oncology section for 20. Many students say he inspired them to become hematologists and oncologists.

■ **Jeff M. Michalski, MD, HS '91**

Faculty Achievement Award

Michalski, the Carlos Perez Distinguished Professor of Radiation Oncology, is a global leader in the treatment of prostate and pediatric cancers. He was honored for his important contributions to radiation oncology and to the improvement of patient care at the Alvin J. Siteman Cancer Center.

■ **Richard W. McCallum, MBBS, HS '72**

Resident/Fellow Alumni Achievement Award

McCallum is professor and founding chair of the Department of Internal Medicine at Texas Tech University Health Sciences Center and chief of its Division of Gastroenterology, Hepatology and Nutrition. He is recognized as a premier thought leader in neurogastroenterology and gastrointestinal motility.

■ **Janet B. McGill, MD, HS '87**

Resident/Fellow Alumni Achievement Award

McGill, a professor of medicine, has made important contributions to further the understanding and management of diabetes mellitus. She has led more than 200 clinical trials and helped develop the most recent American Association of Clinical Endocrinology diabetes treatment guidelines.

Shining example

Ophthalmology department
named for John Hardesty

BY MARY LEE

By all accounts, St. Louis ophthalmologist John Franklin Hardesty, MD (1887-1953), was a hero. As a member of the U.S. Army Medical Corps during World War I, he risked his life to help soldiers on the front lines. After the war, he sent assistance to Polish and Russian soldiers he met while being held as a prisoner of war in Germany. And as a physician, he helped pioneer glaucoma treatments, provided free care to those in need and advocated for laws to benefit the blind.

“When he died, so many people came to his funeral,” said Jane Hardesty Poole, AB ’61, Hardesty’s daughter. “Some of his patients were in tears because he had saved their or their child’s eyesight. My mother and I had no idea he had helped so many people.”



During World War I, Hardesty (seated) helped several soldiers escape from a prisoner of war camp in Villingen, Germany. One of the men, Edouard Issacs (right), who changed his surname to Izac, went on to become a U.S. Congressman from California.

MISSOURI HISTORY MUSEUM, ST. LOUIS

To honor her father's memory and legacy of service, Poole has committed \$10 million to the Department of Ophthalmology and Visual Sciences. In recognition, the department will be renamed the John F. Hardesty, MD, Department of Ophthalmology and Visual Sciences.

"Our department has a long history of advancing understanding of eye diseases and vision loss, particularly in the area of glaucoma," said Todd Margolis, MD, PhD, the Alan A. and Edith L. Wolff Distinguished Professor and department chair. "It is fitting that the department now will bear the name of a man whose life's work involved preserving vision and improving the quality of life for glaucoma patients."

The gift will support ophthalmology research, clinical care and innovative training programs, and will help the department recruit and retain outstanding physician-scientists.

One of 12 children, Hardesty was born in Winfield, Missouri. He earned bachelor's and medical degrees from Saint Louis University in 1914, and completed an internship and residency at St. Louis City Hospital. He had just begun to practice medicine in St. Louis when the U.S. entered World War I in April 1917.

After joining the U.S. Army Medical Corps, Hardesty was among the earliest group of surgeons to volunteer to serve with the British Army as a member of the Seaforth Highlanders, an infantry regiment associated with the northern Highlands of Scotland. During a fierce battle in northwest France, the German Army captured Hardesty while he was manning an aid post on the frontline trenches. For eight months, he was held as a prisoner of war.

Hardesty's role in a daring escape from the Villingen camp in October 1918 was widely reported in newspapers



John Hardesty, MD

after he was honorably discharged from the Army. He devised a successful plan to distract guards and short-circuit lighting along a barbed-wire fence so three fellow prisoners could make their way through it. The Germans never discovered his role in the plot. For his heroism, Hardesty received the Victory Medal.

Hardesty was a faculty member at Saint Louis University Medical School from 1920 until his death, and also served as acting chair of its ophthalmology department.

In 1934, he wrote a thesis for membership in the American Ophthalmological Society that proposed a new way to treat glaucoma using systemic medications such as epinephrine. His research represented the first attempt to treat glaucoma in this way. Epinephrine in eye drop form still is used to treat the disease. Hardesty's work laid the foundation for the development of the oral drug Diamox for glaucoma in the 1950s by Washington University ophthalmology professor Bernard Becker, MD.

Hardesty provided free eye care to residents of the Blind Girls' Home, Missouri School for the Blind and other schools and orphanages, and to patients throughout the region.

Poole, who was only 14 when her father died, remembers him as a kind and loving man. "I adored him," she said. "We would walk down to dinner every night on our wide staircase with our arms around one another. He gave me the unconditional love that every child needs."

"My father was modest and humble," Poole added. "He wanted to be a doctor simply to help people. On top of his great ability, he gave freely of his time and resources. He stands as a shining example of what every doctor should be."

Professor saved eyesight of donor's daughter

In 2012, Jane Hardesty Poole established the John F. Hardesty, MD, Distinguished Professorship in Ophthalmology and Visual Sciences, now held by pediatric ophthalmologist R. Lawrence Tychsen, MD. Poole credits Tychsen with saving her daughter Josephine's eyesight.

Born with a developmental disability, Josephine is non-verbal and could not articulate what she was seeing on traditional eye tests. After consulting many doctors near their Manhattan home, Poole read an article in *The New York Times* highlighting novel ophthalmology treatments at Washington University. In 2004, she and her daughter traveled to St. Louis to meet Tychsen. Through surgery, he restored her vision to 20/40.

The experience convinced Poole that Washington University was the appropriate place to honor her father. "I want to honor him where it's the best," she said. — *Hilary Davidson*



R. Lawrence Tychsen, MD, and Jane Hardesty Poole

Celebrating 100 years

BY HILARY DAVIDSON

MICHELE BERHORST



Cindy Mach, MSOT/MPH/S '17, right, practices functional transfers and safe patient care in an acute care setting, while teaching assistant Brianna Beattie, OTD/S '17, acts as her patient.

Centennial challenge supports scholarships in occupational therapy

The Program in Occupational Therapy is turning 100 years old in 2018. To celebrate, Carolyn Baum, PhD, OTR, FAOTA, the program's Elias Michael Executive Director, has created a scholarship challenge. All gifts to the Occupational Therapy annual fund will be matched by the \$100,000 Carolyn Baum Centennial Challenge, which runs through Dec. 31, 2018.

"At our 100th anniversary, the future of occupational therapy has never looked brighter," Baum said.

Baum said she hopes the challenge will inspire alumni and friends to make a special gift, ensuring that the best and brightest students become the health-care leaders of tomorrow.

"The Baum Centennial Challenge lays the groundwork for another 100 years of superlative teaching and research at the Program in Occupational Therapy," said

"At our 100th anniversary, the future of occupational therapy has never looked brighter." — Carolyn Baum, PhD

David H. Perlmutter, MD, executive vice chancellor for medical affairs and dean of the School of Medicine.

To learn more, visit medicalalumni.wustl.edu/baumcentennialchallenge.

About Carolyn Baum

Baum, a professor of occupational therapy, neurology and social work, has led the occupational therapy program since 1988.

Her interdisciplinary perspective has helped guide the program, which U.S. News & World Report ranks as No. 1 in the nation. In 2017, the American Occupational Therapy Association named Baum as one of 100 influential people who have shaped the field of occupational therapy.

Baum earned a bachelor's degree in occupational therapy from the University of Kansas, a master's degree in health management from Webster University, and a doctorate in social work from the Brown School at Washington University.



Carolyn Baum, PhD

ROBERT BOSTON

Find your friends.

Classnotes are organized first by year of degree/training completion and then in alphabetical order.

How about you?

Share your news via the online form at wumcnews.org/classnotes. Submissions will be printed in a subsequent issue of Outlook magazine as space allows. Photos are welcome.

1950s



Emil Mantini, MD '58, and his wife, **Jane Mantini, NU '57**, moved to Tampa, Fla., where they enjoy living in an active senior center and watching

sailboats gather in the bay once a week. They have three grown children: sons Franz and Louis, who live in Tampa and northern Florida, respectively, and daughter Elizabeth, who lives in the St. Louis area. The family recently gathered in Tampa to celebrate the couple's 60th wedding anniversary.

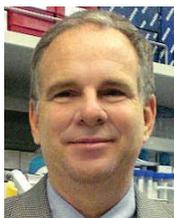
1960s

Robert D. Porter, MD '67, retired from nephrology practice in Topeka, Kan. In 2013, he received the Bal Jeffrey Award for advancing medical care in northeast Kansas. Porter continues to serve as a senior Federal Aviation Administration aeromedical examiner and as a short-term medical provider to the Karen people along the Thai-Burma border. He is also a regular volunteer at the Abilene and Smoky Valley Railroad in Abilene, Kan.

Virginia Crandall, NU '69, returned to work, providing women's health care two days a week at a private practice in Colorado Springs, Colo. She also enjoys traveling and recently took a bike tour of New Zealand with friends and her daughter and son-in-law.

1970s

Thomas H. Gee, HA '78, recently was recognized for 25 years of service as the chief executive officer of Henry County Medical Center in Paris, Tenn. Gee serves on the Board of Directors of the Tennessee Hospital Association and as an alternate delegate to the American Hospital Association. In 2016, Governor Bill Haslam appointed Gee to the Tennessee State Board for Licensing of Health Care Facilities.



Stephen Young, MD '78, was elected to the National Academy of Sciences in 2016 for his research on plasma lipid metabolism and diseases of the nuclear envelope. He is a cardiologist and

distinguished professor of medicine and human genetics at the David Geffen School of Medicine at UCLA.

1980s

Molly Eaton, MD '81, spent more than 30 years in Atlanta and is moving to Denver to serve as associate professor in infectious diseases at the University of Colorado Health Sciences Center, Anschutz Medical Campus.

David Pfeffer, MD '83, is president of The Virginia Urological Society. He also serves as the Virginia State Society representative to the American Association of Clinical Urologists. He would like to encourage his former classmates to become politically engaged, both on a state and national level. He continues to practice independently in Warrenton and Culpeper, Va.

Jon R. Friedman, MD '84, recently was inducted as a fellow of the American Society of Transplantation (AST) at the American Transplant Congress in Chicago and received a Distinguished Service Award from the AST in 2016. He is chief medical officer for Optum's Population Health Solutions programs. Optum is the health services division of UnitedHealth Group.



Elizabeth Reed Hanson, MD/GM '07, and **Scott Hadland, MD '09**

Alumni honored for teaching

The Academic Pediatrics Association (APA) honored two Washington University alumni at its recent Pediatric Academic Society meeting in San Francisco. Elizabeth Reed Hanson, MD/GM '07, assistant professor/clinical and associate program director of the Pediatric Residency Program at the University of Texas Health Science Center, San Antonio, received the APA Teaching Award for Faculty (Junior). Scott Hadland, MD '09, director of the Urban Health and Advocacy Track of the Boston Combined Residency Program at Boston Medical Center and Boston Children's Hospital, received the Residency Teaching Program Award.

James F. Loomis Jr., HS '88, EMBA '97, recently moved to Washington, D.C., to become medical director at Barnard Medical Center, a non-profit primary care medical practice that focuses on nutrition to help prevent, treat and reverse many chronic diseases.

1990s

Steve A. Harvey, LA '88, MD '92, HS '96, has been working to build TMS St. Louis, a psychiatric subspecialty practice that provides transcranial magnetic stimulation (TMS) for patients with moderate or severe treatment-refractory depression.

Ari Berkowitz, GM '93, professor of biology at the University of Oklahoma, wrote and published a neurobiology book for a general audience, titled "Governing Behavior: How Nerve Cell Dictatorships and Democracies Control Everything We Do," from Harvard University Press.

Ajay Ahuja, MD '95, recently took a role at Allergan Global as head of global and U.S. medical affairs. Ahuja will move with his family from Chicago to the New York City area, where the company is headquartered.

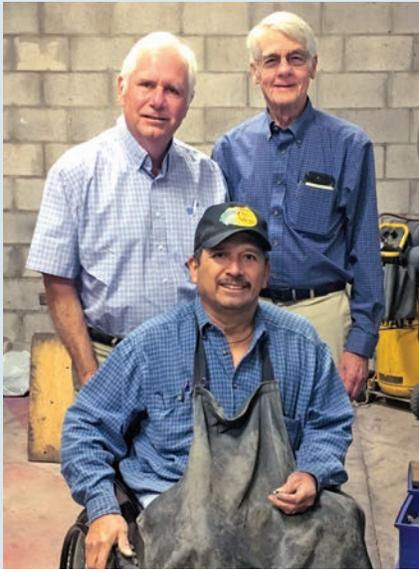
Michael Finley, PhD '98, principal scientist at Janssen R & D in Spring House, Pa., leads a team of assay-development scientists in a newly revitalized high-throughput screening group for small-molecule drug discovery. This supports a range of therapeutic areas, including oncology, immunology and neuroscience. Fellow classmate and spouse, **Audrey Ettinger, PhD '98**, is completing a first sabbatical semester after 15 years as a faculty member at Cedar Crest College in Allentown, Pa. In addition to her ongoing research and teaching commitments, Ettinger serves as an instructor in the Greater Allentown Math Science Partnership to bring inquiry-based

teaching methods to seventh-12th grade teachers in the Allentown school district. Their children, Raphael, 14, and Julian, 10, are completing ninth and fifth grades, respectively.

Mary Iovine, PhD '98, recently was promoted to professor at Lehigh University in the Department of Biological Sciences.



Joni M. Kamiya, OT '99, participated in the 2015 Cornell Alliance for Science Global Leadership Fellows Program to help advocate for science-based policies and access to technology. Kamiya lives in Honolulu, and works professionally with senior adults and people with disabilities.



Clockwise from top left: William Neubauer, MD '69; Burris "Duke" Duncan, BA '54, MD; and wheelchair expert Gabriel Zepeda.

Nonprofit empowers Mexicans with disabilities

Two Washington University alumni are helping hundreds of Mexican children and adults with disabilities obtain affordable prosthetic limbs, all-terrain wheelchairs and solar-powered hearing aids.

Realizing the great need for these devices among low-income Mexicans, Burris "Duke" Duncan, BA '54, MD, established the nonprofit company Arizona Sonora Border Projects for Inclusion (ARSOBO) in 2012. William Neubauer, MD '69, who retired after 30 years as a general surgeon, now serves as the nonprofit's board chair.

"If you lose a leg in Mexico, you are on crutches for life because prosthetics are extremely expensive," Neubauer said.

ARSOBO promotes self-sufficiency by training and employing individuals with disabilities to construct medical equipment for themselves and others. These individuals are charged only the cost of the device, or what they can afford. ARSOBO recoups the remaining cost through charitable donations.

Neubauer has witnessed many miracles: adults who now work and lead normal lives; an 8-year-old who learned to talk after getting a hearing aid; and formerly homebound children with cerebral palsy who attend school.

"This is as important and satisfying to me as my 30 years in surgery," Neubauer said.

Rebecca S. Sippel, MD '99, associate professor and chief of the Division of Endocrine Surgery at the University of Wisconsin-Madison, is serving as president of the Association for Academic Surgery for the 2017-18 term.



2000s



Jeffrey Henderson, MD/PhD '02, was promoted to associate professor of medicine and molecular microbiology at WUSM and elected to the American Society for

Clinical Investigation. Henderson also received the Washington University Outstanding Faculty Mentor Award from the Graduate Student Senate.

Rachel Sieber, OT '05, recently received a post-professional doctorate in occupational therapy from George Washington University.

Cawas Engineer, PhD '06, completed a successful research project on crop abiotic stress signaling at the University of California, San Diego, and recently accepted the role of director of research at a start-up company in San Diego, where he will lead research on sensory input perception for drug discovery.

Keydra L. Oladapo, GM '06, is currently serving a four-year term as U.S. diplomat in Southern Africa and received a promotion to branch chief of epidemiology, surveillance, monitoring and evaluation at the Centers for Disease Control and Prevention.

Stacy Kruse, LA '03, MD '08, recently returned to the U.S. with her husband and 3-year-old son, after two and a half years of living in England. They have settled near Washington, D.C., where Stacy is an assistant professor of clinical medicine at MedStar Georgetown University Hospital.

Kimberly Dale, OT '09, was selected to participate in the Veterans Administration's Clinical and Administrative Leadership Development Institute. This is a competitive training and development program aimed at building leadership skills for higher roles in a health-care system. Dale lives in Detroit.

2010s

Tassy Hayden, LA '07, MD '11, is joining the staffs of Southampton Healthcare in St. Louis and BJC HealthCare. She looks forward to aiding in the education of WUSM students and serving the LGBT and HIV-positive communities, particularly.

Aaron M. Bertoni, MD '12, completed residency training in anesthesia at the University of Washington, Seattle, and works part time at Island Hospital in Anacortes, Wash. He spends the rest of his time sailing the San Juan Islands, hiking the Pacific Crest Trail and crabbing in Puget Sound with his wife, Emily, and dog, Barney.

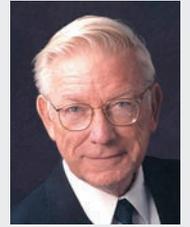
Raghav Govindarajan, HS '13, recently gave four invited talks and was awarded the Clerkship Director Teaching Award, the A.B. Baker Teacher Recognition Award and the Patient Safety Award by the American Academy of Neurology at its national meeting in Boston. He is assistant professor of neurology at the University of Missouri-Columbia School of Medicine.



Louis Poppler, GM '15, will begin a fellowship at the Mayo Clinic for advanced training in hand and nerve surgery.

Darlene R. (Gollaher) Tilley, PT '15, married Matthew Tilley, a student at Covenant Theological Seminary, in 2016. She is celebrating two years of employment at SSM Health Physical Therapy and pursuing a certified strength and conditioning specialty.

Robert C. Drews, MD '55, a professor emeritus of clinical ophthalmology, former member of the Board of Trustees and university benefactor, died Tuesday, May 9, 2017, at his home in St. Louis, following a stroke. He was 86.



Drews was an ophthalmologist, photographer, inventor of numerous medical instruments for the eye, and author of more than 500 journal articles, book chapters and books.

"His expertise in lens implantation and cataract surgery gained him international recognition and numerous invitations to teach advanced ophthalmic microsurgical techniques all over the world," said Todd P. Margolis, MD, PhD, the Alan A. and Edith L. Wolff Distinguished Professor and head of the Department of Ophthalmology and Visual Sciences.

Drews graduated from the School of Medicine in 1955, did a residency in ophthalmology from 1956 to 1959, and became chief resident in 1958. After residency, he entered the Navy, serving at the U.S. Naval Hospital, Great Lakes, before returning to St. Louis to go into private practice and teach in the Department of Ophthalmology.

He is survived by his daughters Pamela Breitberg (Steven), Belinda Laupp and Jeanmarie Mertens (John); son, Carl Drews (Deborah); 10 grandchildren and eight great-grandchildren. His wife, Lorene, preceded him in death.



Frederick D. Peterson, MD, a former professor of clinical pediatrics, died Thursday, March 2, 2017, in his sleep at a nursing home in Chesterfield, Mo. He was 85.

A longtime influential presence at St. Louis

Children's Hospital, Peterson began his affiliation with the university in 1957 as an intern and ultimately ascended to professor of clinical pediatrics in 1992. Peterson also maintained a private practice for more than three decades.

Peterson is survived by his brother, William Peterson, of Tallahassee, Fla.

continued on page 36 ...



John M. Fredrickson, MD, former head of the Department of Otolaryngology, died Wednesday, April 5, 2017, in Vancouver, Canada. He was 86.

Fredrickson came to Washington University in 1982 to serve as the Lindburg Professor and head of the Department of Otolaryngology, a position he held until 1998. He became an emeritus professor in 2002.

Under Fredrickson's leadership, the department grew in both clinical and research activities. His body of research included major contributions to the fields of vestibular neurophysiology, middle-ear implants and microvascular reconstructive surgery of the head and neck. After his retirement in 2002, Fredrickson returned to Vancouver and remained active in the field, helping to develop an implantable transducer for severe hearing loss.

Fredrickson is survived by his wife, Alix, and his three children, Kristin, Lisa and Erik Fredrickson.



Travis C. Mazer, a doctoral candidate studying molecular genetics and genomics, died unexpectedly Monday, April 24, 2017, in St. Louis. He was 25.

His research focused

on lysosomal biology in cellular stress and homeostasis, with a goal of understanding pathways to enhance cellular longevity. He worked in the lab of Abhinav Diwan, MD, an associate professor of medicine, and will be listed as an author on an upcoming research paper from Diwan's lab.

Earlier, he worked for two years as a research technician in the lab of Zachary Pincus, PhD, an assistant professor of developmental biology and genetics.

A Kalamazoo, Mich., native, Mazer earned a bachelor's degree in neuroscience from the University of Michigan.

He is survived by his parents, Wendy and Kevin Mazer; sisters, Mallory and Madison; brothers, Taylor, Trent (Kaitlin) and Tate; grandmothers, Jacqueline Roberts and Joyce Griffin, plus many aunts, uncles and cousins.



Jean Holowach Thurston, MD, a pioneering pediatric neurologist, died Saturday, April 29, 2017. She was 99 and about a month away from her centennial birthday. Thurston died of natural causes at a retirement home in University City, Mo.

A professor of pediatrics and of neurology, Thurston's influential research has guided treatment of childhood seizure disorders. She led long-term studies examining anticonvulsant withdrawal in pediatric patients with epilepsy. Thurston's research, published in 1972 in *The New England Journal of Medicine*, identified seizure recurrence risks. Those findings, which remain relevant today, contributed to therapies and diagnostic tools for childhood epilepsy.

Thurston continued her research for decades, establishing a neurochemistry lab, publishing her last paper at age 78 and attending professional seminars until a year before her death.

Thurston is survived by eight nieces. She was preceded in death by her husband of 38 years, Donald L. Thurston, MD, a professor emeritus of pediatrics. The couple collaborated on multiple research projects.

1940s

Ernest J. Clark, MD '48; Nov. '16
Frank X. Dwyer, MD '43; Feb. '17
Robert H. Hall, MD '45; March '17
Dolores M. Moore, PT '48; Feb. '17
Betty Jo Petrofsky, NU '48; Jan. '17
Thomas E. Prosser III, DE '45; April '17
Clarence G. Schulz, MD '45; Nov. '16

1950s

Eric I. Anderson, MD '52; Jan. '17
Ruth C. Comens, MD '50; Feb. '17
Henry R. Dallam Jr., DE '54, GD '64; Jan. '17
Floyd M. Freeman, DE '54; Feb. '17
Dwayne R. Good, DE '57; Dec. '16
Howard R. Gray, MD '52, HS; Feb. '17
William G. McCuen, HS '55; March '17
Ralph B. Montgomery, DE '54; March '17
Marian P. Paxhia, NU '57; March '17
Jack Baer Rosen, LA '55, DE '58; March '17
Raymond G. Schultze, LA '55, MD '59, HS '63; April '17
Richard E. Thompson, MD '59; Jan. '17
Betty McKee Von Rump, PT '58; Feb. '17

1960s

Henry E. Dupree, DE '63; April '17
Allan P. Fishbein, MD '64; Sept. '16
Koichi Fujii, HS '62; March '17
Gerald L. Howell, DE '60; May '17
Charles B. Manley, HS '67; Nov. '16
Thomas E. O'Keeffe, DE '69; Feb. '17
Nancy L. Pope, NU '66; March '17
Arthur Schneider, LA '57, MD '61; May '17
Eli R. Shuter, MD '60; April '17
Thomas W. Yager, DE '64; Feb. '17

1970s

Barry Miller Farr, MD '78; Feb. '17
Kay Miller Rusche, MD '77; Feb. '17
Ernest P. Sutton, DE '73; April '17
Anthony Weisenberger, MD '71; March '17

1980s

Alexandre Carli, HS '83; Jan. '17
David Bradley Marrs, HS '82; March '17

2000s

Aaron Rogat, PhD '02; April '17

For full obituaries, visit:
wumcnews.org/obits

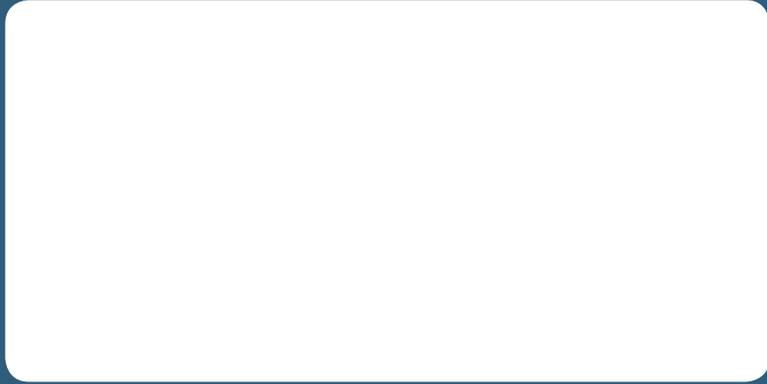


Magical moment

Second-year medical student Hayley Motowski, dressed as Belle from “Beauty and the Beast,” presents a rose to Sarah Norwood, 9, of Arkansas, who was awaiting surgery at St. Louis Children’s Hospital. Students practicing for the 12th annual School of Medicine musical — including (bottom, from left) Molly Grabill as Mrs. Potts, Motowski, Chase Elwood as the Beast and Philip Frasse as Lumiere — took their act to the hospital. While there, Motowski even demonstrated a proper princess wave. Sarah’s mom, Sherri Norwood, called the visit a welcome distraction.

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Witnessing history

The Washington University community gathered at Ellen S. Clark Hope Plaza to watch as the solar eclipse reached 99.99 percent totality on the Medical Campus.



KAREN LSHOOT