Public health's defense teams work behind the scenes

Controlling OUTBREAKS
Improving the lives of babies

Michele Imel-Kebe holds her twin daughters, Bella Imel-Thompson, left, and Ava Imel-Thompson, at St. Louis Children’s Hospital. Bella and Ava were born seven weeks early. Imel-Kebe is hopeful that a prematurity research center launched Nov. 10 by Washington University, Children’s Hospital and the March of Dimes will achieve major milestones to help bring more babies to term. The March of Dimes Prematurity Research Center at Washington University in St. Louis is one of a handful of centers nationwide that is studying the causes of preterm birth.
Reconstructing an active lifestyle

Infectious diseases faculty members Rupa Patel, MD, MPH, DTM&H, and Steven J. Lawrence, MD, MSc, wear personal protective equipment during an Ebola preparedness session. For months, BJC infection preventionists have been training frontline nurses and doctors like Patel and Lawrence. Because of the extreme care that must be taken to remove the gear and prevent self-contamination, these intensive sessions are conducted in small groups. To learn more about infectious disease efforts, see page 21.

Inspired by Saturday

Medical students apply their classroom skills toward real-world health-care needs in the heart of the city.

Restoring joy

Understanding early childhood depression could alter the course of a life.

Windows into ancient lives

Three mummies arrive for checkups, offering enduring lessons in art, science and humanity.

The best defense

Vigilance, research and response to the threat of infectious disease.

Cover

Infectious diseases faculty members Rupa Patel, MD, MPH, DTM&H, and Steven J. Lawrence, MD, MSc, wear personal protective equipment during an Ebola preparedness session. For months, BJC infection preventionists have been training frontline nurses and doctors like Patel and Lawrence. Because of the extreme care that must be taken to remove the gear and prevent self-contamination, these intensive sessions are conducted in small groups. To learn more about infectious disease efforts, see page 21.

Image by Robert Boston and Eric Young
Scientists have described a way to convert human skin cells directly into medium spiny neurons that are important for controlling movement. These are the primary cells affected in Huntington's disease. Unlike other techniques that turn one cell type into another, this new process does not involve passage through a stem cell phase, and avoids the production of multiple cell types.

In the study, researchers converted adult human skin cells into medium spiny neurons with exposure to the right combination of chemical signals. They then injected these converted cells into mice brains.

Reporting in the journal Neuron, the researchers showed that these converted cells survived at least six months after injection into mice brains and behaved similarly to native cells in the brain. “Not only did these transplanted cells survive in the mouse brain, they showed functional properties similar to those of native cells,” said senior author Andrew S. Yoo, PhD, assistant professor of developmental biology.

The ability to convert adult human cells may launch future therapies using a patient’s own easily accessible cells. In a skin cell, the DNA instructions for how to be a brain cell, or any other type of cell, is neatly packed away, unused. In past research published in Nature, Yoo and his colleagues showed that exposure to two microRNAs (miR-9 and miR-124) altered the machinery that governs packaging of DNA. Though the investigators still are unraveling the complex details, these microRNAs appear to be opening up the tightly packaged sections of DNA important for brain cells, allowing expression of neuronal genes.

Knowing these microRNAs could change skin cells into a mix of neurons, the researchers finetuned the chemical signals, exposing the cells to additional molecules called transcription factors, which are present in the part of the brain where medium spiny neurons are common. The investigators showed that the transcription factors guide the skin cells to become a specific subtype of neuron.
Schizophrenia

Its genetic complexity revealed

New research shows that schizophrenia isn’t a single disease but a group of eight genetically distinct disorders, each with its own set of symptoms. The finding could be a first step toward improved diagnosis and treatment for the debilitating psychiatric illness. The research is reported online in The American Journal of Psychiatry.

About 80 percent of the risk for schizophrenia is known to be inherited, but scientists have struggled to identify specific genes for the condition. Now, in a novel approach analyzing genetic influences on more than 4,000 people with schizophrenia, the research team has identified distinct gene clusters that contribute to eight different classes of schizophrenia.

“Genes don’t operate by themselves,” said C. Robert Cloninger, MD, PhD, one of the study’s senior investigators. “They function in concert much like an orchestra, and to understand how they’re working, you have to know not just who the members of the orchestra are but how they interact.”

Cloninger, the Wallace Renard Professor of Psychiatry and Genetics, and his colleagues matched precise DNA variations in people with and without schizophrenia to symptoms in individual patients.

Although individual genes have only weak and inconsistent associations with schizophrenia, groups of interacting gene clusters create an extremely high and consistent risk of illness, on the order of 70 to 100 percent. That makes it almost impossible for people with those genetic variations to avoid the condition. In all, the researchers identified 42 clusters of genetic variations that dramatically increased the risk.

“In the past, scientists had been looking for associations between individual genes and schizophrenia,” explained Dragan M. Svrakic, PhD, MD, a co-investigator and a professor of psychiatry. “When one study would identify an association, no one else could replicate it. What was missing was the idea that these genes don’t act independently. They work in concert to disrupt the brain’s structure and function, and that results in the illness.”

Vice chancellor for research appointed

Jennifer K. Lodge, PhD (’88), associate dean for research and professor of molecular microbiology at the School of Medicine, has been appointed as the university’s vice chancellor for research. Chancellor Mark S. Wrighton; Larry J. Shapiro, MD, executive vice chancellor for medical affairs and dean of the School of Medicine; and H. Holden Thorp, PhD, provost and executive vice chancellor for academic affairs, made the announcement.

Lodge succeeds Evan Kharasch, MD, PhD, the Russell D. and Mary B. Shelden Professor of Anesthesiology and professor of biochemistry and molecular biophysics, who has served in the role since 2009.

Lodge will continue as associate dean for research at the medical school. She has coordinated efforts to advance medical school research, focusing on interdisciplinary projects with core facilities that serve a wide variety of researchers. Lodge assists faculty in identifying funding opportunities and maximizing the benefits of school-wide research investments.

In her new role, Lodge will serve as an officer of Washington University and a member of the University Council. As chief officer responsible for the university’s research mission, she oversees more than $600 million in annual sponsored research and manages the development of research policies, grants and contracts, and the continuing education of faculty and staff regarding research regulations.
Orthopaedic surgery chief named

Regis J. O’Keefe, MD, PhD, has been named head of the Department of Orthopaedic Surgery. With the new appointment, O’Keefe also became orthopaedic surgeon-in-chief at Barnes-Jewish and St. Louis Children’s hospitals.

“I am pleased to welcome Regis O’Keefe, who is a national leader in musculoskeletal research and clinical care delivery in orthopaedics,” said Larry J. Shapiro, MD, executive vice chancellor for medical affairs and dean of the School of Medicine.

A highly regarded orthopaedic oncologist, O’Keefe comes to St. Louis from the University of Rochester School of Medicine and Dentistry, where he was the Marjorie Strong Wehle Professor in Orthopaedics and chair of the Department of Orthopaedics and Rehabilitation. He also was associate dean for clinical affairs and a professor of pathology and laboratory medicine and of biochemistry and biophysics.

O’Keefe’s practice focuses on patients with tumors in bones, joints and soft tissue. He also treats patients with fractures that result from brittle bones due to osteoporosis, osteopenia and other bone diseases.

O’Keefe succeeds Richard H. Gelberman, MD, who became the head of orthopaedic surgery at the department’s inception in 1995. Under Gelberman’s leadership, the department became nationally recognized. Now it is a top recipient of funding from the National Institutes of Health (NIH).

A renowned hand and wrist surgeon, Gelberman will maintain his clinical practice and continue to pursue research.

These little piggies went to med school

While some School of Medicine employees were content with pulled-pork sandwiches at the annual employee appreciation picnic, others showed their competitive spirit and wagered on animated, stuffed-pig races. The picnic, sponsored by the dean’s office and the Medical School Management Council, was held in September. Despite unreasonably cool temperatures, hundreds turned out for fun and games in Hudlin Park.

Don’t scratch!

Yes, it really does make itching worse

Turns out your mom was right: Scratching an itch only makes it worse. New research indicates that scratching causes the brain to release serotonin, which intensifies the itch sensation.

The findings, in mice, are reported online in the journal Neuron. The same vicious cycle of itching and scratching is thought to occur in humans, and the research provides new clues that may help break that cycle, particularly in people who experience chronic itching.

Scientists have known for decades that scratching creates a mild amount of pain in the skin, said senior investigator Zhou-Feng Chen, PhD, director of the university’s Center for the Study of Itch. That pain can interfere with itching — at least temporarily — by getting nerve cells in the spinal cord to carry pain signals instead of itch signals to the brain.

“The problem is that when the brain gets those pain signals, it responds by producing the neurotransmitter serotonin to help control that pain,” Chen said. “But as serotonin spreads from the brain into the spinal cord, we found the chemical can ‘jump the tracks,’ moving from pain-sensing neurons to nerve cells that influence itch intensity.”

The researchers bred a strain of mice that lacked the genes to make serotonin. When those genetically engineered mice were injected with a substance that normally makes the skin itch, the mice didn’t scratch as much as their normal littermates.

When the genetically altered mice were injected with serotonin, they scratched as might be expected in response to itch-inducing compounds.

However, Chen said it’s not practical to treat itching by blocking serotonin release. Serotonin is involved in growth, aging, bone metabolism and in regulating mood. Blocking serotonin would have consequences throughout the body, and people wouldn’t have a natural way to control pain.

Instead, it might be possible to interfere with the communication between serotonin and nerve cells in the spinal cord that specifically transmit itch. To work toward that goal, Chen’s team isolated the receptor used by serotonin to activate these neurons.
More than 3 million pregnant women give birth annually in the U.S. But physicians still know little about the best ways to manage the crucial second stage of labor, the stage that is the hardest physically on mothers and babies.

Difficulties can lead obstetricians to recommend C-sections rather than vaginal deliveries. As women begin the second stage of labor, most are urged to push as soon as the cervix has dilated to 10 centimeters. A competing theory holds that women should delay pushing until they feel the urge to push.

With support from an $8.7 million National Institutes of Health (NIH) grant, School of Medicine researchers will collect and analyze data on how to best manage the second stage of labor. The five-year grant is funding a trial involving 3,400 women at six U.S. hospitals.

"Many current practices in labor and delivery have come from tradition," said Alison G. Cahill, MD, co-principal investigator of the study and associate professor of obstetrics and gynecology. "Many providers believed that delayed pushing would improve rates of vaginal delivery and reduce infant complications. But when we looked at past studies, delayed pushing, compared with immediate pushing, sometimes caused more problems for babies."

Previous studies comparing these two approaches involved small numbers of patients or obsolete practices and often reported contradictory results.

In the current study, women will be randomly assigned to two groups. Women in one group will be asked to begin pushing as soon as the cervix is fully dilated. Women in the second group will be instructed to wait for 60 minutes after the cervix is dilated to begin pushing.

Cahill and Methodius G. Tuuli, MD, co-principal investigator and assistant professor of obstetrics and gynecology, will assess the timing of pushing on the rate of vaginal and C-section deliveries. "Current C-section rates are of great concern," said Cahill, who along with Tuuli delivers babies at Barnes-Jewish Hospital. "C-sections are performed for a number of reasons. If we start solving some of these problems and help women deliver their babies vaginally, we can lower the C-section rates."

The researchers also will determine if immediate or delayed pushing reduces the rates of serious neonatal infections, lung problems and neonatal intensive care admissions. Additionally, Cahill and Tuuli will use ultrasound to evaluate the effects of immediate versus delayed pushing on pelvic floor injuries.

Participating hospitals include: Barnes-Jewish Hospital, Missouri Baptist Medical Center, Oregon Health & Science University Hospital, Hospital of the University of Pennsylvania, Pennsylvania Hospital, and the University of Alabama in Birmingham Hospital.
Anyone who has suffered from kidney stones is keenly aware of the lack of drugs to treat the condition, which often causes excruciating pain.

A new mouse study, however, suggests that a class of drugs approved to treat leukemia and epilepsy also may be effective against kidney stones. The drugs are histone deacetylase inhibitors, or HDAC inhibitors for short. The researchers found that two of them — Vorinostat and trichostatin A — lower levels of calcium and magnesium in the urine. Both calcium and magnesium are key components of kidney stones.

The research is available online in the journal of the American Society of Nephrology.

“We’re hopeful this class of drugs can dissolve kidney stones because its effects on reducing calcium and magnesium are exclusive to kidney cells,” said senior author Jianghui Hou, PhD, assistant professor of medicine. “In the mice, we achieved dramatic effects at a fraction of the dosage used to treat leukemia and without significant side effects.”

Most kidney stones form when the urine becomes too concentrated, allowing calcium and magnesium to crystallize and stick together. Intense pain develops when stones get stuck in the urinary tract and block the flow of urine.

Diet can play a role in the condition. Not drinking enough water or eating a diet with too much salt, which promotes calcium to be released into the urine, increases the risk of stones. Some people also are genetically prone to developing kidney stones, and they naturally release too much calcium into the urine.

Typically, doctors recommend drinking lots of water to help pass kidney stones from the body. Thiazide, a drug used to treat high blood pressure, sometimes is prescribed to treat the stones because it reduces calcium in the urine. But the drug also increases magnesium in urine, countering its effectiveness against kidney stones.
The Missouri River 340 is not your father's float trip. This grueling race pits paddlers against a swift 340-mile stretch of the Missouri River that winds from Kansas City to St. Louis.

Among the 2014 competitors was Joan Twillman, 60, a retired high school chemistry teacher who lives in St. Charles, Missouri. She and seven other women completed the August race by paddling 55 hours non-stop in a 30-foot canoe. The "Ladies & Clark" team placed second in its division; typically a third of the race competitors do not even finish.

Navigational challenges — fog, the hot sun by day and darkness at night, parked barges, submerged trees and floating obstacles — quickly cull the pack. Fatigue, pain and stress take their toll.

Twillman, a Missouri Master Naturalist, has competed regionally, led daylong kayaking excursions for a local canoe club and even ziplined in Costa Rica, all while undergoing reconstructive treatment following breast cancer.

She credits surgeon Terence M. Myckatyn, MD, associate professor of plastic and reconstructive surgery and director of cosmetic and breast plastic surgery at the School of Medicine, with understanding her active lifestyle and offering personalized treatment.

Following a mastectomy in 2010, Twillman, a wife, mom and grandmother, had no plans for breast reconstruction, fearing that additional surgeries would prolong her ordeal. But, traveling and exercising with prosthetics proved too cumbersome.

Myckatyn explained reconstruction options, including an advanced surgery not widely available — transplantation of fat, skin and blood vessels from the patient's abdomen.

After consideration, Twillman and Myckatyn took a "less is more" approach, deciding saline implants would better spare the critical muscles needed for kayaking.

She underwent a surgery to insert tissue expanders, a series of saline fills and, finally, a surgery to place permanent implants; all of the procedures were built around her busy schedule.

"He worked with me every step of the way during recovery and my return to competition, even going at a slower pace or taking breaks as needed. Going to Costa Rica, he realized, was more important. "The reconstruction was a big part of making me feel that I am no longer a cancer patient."
Researchers have developed algorithms to identify weak spots in tendons, muscles and bones prone to tearing or breaking. The technology, which needs to be refined before it is used in patients, one day may help pinpoint minor strains and tiny injuries in the body’s tissues long before bigger problems occur. The research is available online in the Journal of the Royal Society Interface.

“Tendons are constantly stretching as muscles pull on them, and bones also bend or compress as we carry out everyday activities,” said senior investigator Stavros Thomopoulos, PhD, professor of orthopaedic surgery. “Small cracks or tears can result from these loads and lead to major injuries. Understanding how these tears and cracks develop over time is important for diagnosing and tracking injuries.”

Thomopoulos and his colleagues developed a way to visualize and even predict spots where tissues are weakened. To accomplish this, they stretched tissues and tracked what happened as their shapes changed or became distorted.

The paper’s first author, John J. Boyle, a graduate student in biomedical engineering, combined mechanical engineering fundamentals with image-analysis techniques to create the algorithms, which were tested in different materials and in animal models.

“If you imagine stretching Silly Putty or a swimming cap with a picture on it, as you pull, the picture becomes distorted,” Boyle said. “This allows us to track how the material responds to an external force.”

One of the two new algorithms is 1,000 times more accurate than older methods at quantifying very large stretches near tiny cracks and tears. And a second algorithm has the ability to predict where cracks and failures are likely to form.

Thomopoulos, who also is a professor of biomedical engineering and of mechanical engineering, and Guy Genin, PhD, professor of mechanical engineering and co-senior investigator, want to learn why some surgeries to repair rotator cuff injuries ultimately fail. In the long run, they want to use the algorithms to prevent additional injuries following surgery to repair knees, shoulders and other tissues.
The Saturday Neighborhood Health Clinic makes a difference in the lives of its patients and the medical students who care for them.
The first line started 17 years ago:
Men and women shivering on an overcast Saturday in January in a partly abandoned swath of St. Louis City.

Only 10 degrees outside and not even 9 a.m., the underserved and uninsured waited by the nondescript building in the Forest Park Southeast neighborhood. They might have coughed or ached or itched, but all were hopeful for the chance to see a doctor.

For free.

The line has continued for almost every Saturday morning since, serving as a constant in the neighborhood throughout the year’s changing seasons and the community’s ongoing revitalization efforts.

The wait is for the Saturday Neighborhood Health Clinic, which operates on a first-come, first-served basis from 9 a.m. to noon. Students at Washington University School of Medicine run the clinic with help from a volunteer board-certified physician.
Housed in the Family Health Care Center on Manchester Avenue, the federally qualified clinic offers no-cost, episodic health services similar to those available at a primary care provider’s office: treatment of acute or chronic medical conditions, preventative care, vaccinations, women’s health care, physical exams and prescription refills, often free or at a reduced cost. It does not provide pediatric or dental care but refers patients to organizations that can help.

Despite the high demand, the Saturday clinic only has the funding, staffing and space to help the first nine patients in line.

“It is heart-wrenching to turn people away,” said Will Ross, MD, MPH, associate dean for diversity and associate professor of medicine at Washington University School of Medicine who also started the Saturday clinic, chartering it in September 1996 and opening it the following winter. “A lot of people who come to clinic have jobs to go to on Saturdays or take buses to get here. Bus fares, even a few dollars, can be a big expense, and then to have to turn them away after all their efforts to get here, well, gosh, it’s hard.”

Better to focus on the many lives it helps — up to 400 a year and approximately 7,200 since its inception — and all with an annual budget of $25,000. “A lot of these people have gone years without seeking health care,” Ross said recently in his office, where more than a dozen awards hang on the wall, many for humanitarianism. “Some people don’t get help until their condition worsens and then they’re likely to seek help at a hospital emergency room. The cost is high to both the patient, who cannot afford the medical bills, as well as to overall health-care costs for consumers.”

The clinic does not provide long-term patient care; rather, Ross called it a “stop-gap measure” for ailments such as Type II diabetes, sexually transmitted infections, asthma, high blood pressure and, the most common, chronic back pain typically caused by labor-intensive jobs. The hope is that patients needing follow-up care will pursue it with resources offered through the clinic.

Besides providing health care, Ross said the Saturday Neighborhood Health Clinic gives medical students the opportunity to serve the community while also learning about public health through a practical, hands-on clinical experience.

Each Saturday, the clinic deploys at least three medical teams composed of preclinical and clinical students. Specifically, a team consists of one first- or second-year student and one third- or fourth-year student. Any medical student may volunteer at the clinic. As of last year, Ross said, 90 to 95 percent of students had volunteered at the clinic during medical school.

A student coordinator is also part of the team. To reach this level, students must enroll in a selective class Ross teaches called “Healthcare Management: Saturday Neighborhood Health Clinic,” which focuses on public health issues, with an emphasis on the urban health-care needs in St. Louis.

A volunteer Washington University physician supervises all students. The physician helps to determine a patient’s diagnosis and treatment, provides guidance as students conduct patient interviews, oversees patient flow, manages charts and paperwork and sometimes performs physical exams, among other tasks.
The clinic often inspires students to make life-changing career choices. “Working at the clinic has given me an intimate view of the pressing social challenges we’re facing in health care in St. Louis,” said Kevin Baumgartner, a fourth-year student who spent two years there and is currently applying for residencies in emergency medicine. “I helped take care of hard-working people who, through no fault of their own, have no jobs, insurance or transportation. I saw firsthand how our current health-care system fails our neediest citizens. This experience has helped motivate me to dedicate my career as a physician to improving safety-net health care and advocating for the vulnerable.”

Baumgartner recalled one clinic patient, in particular, who reaffirmed his career path: “An older man came in with what was almost certainly a blood clot in his leg. We urged him to go straight to the ER, by ambulance if necessary, as these clots can break off and lodge in the lung if not treated properly, which can cause respiratory failure, heart failure and even death. But the man refused to go. He had no insurance or money and didn’t think he could run the financial risk of a trip to the hospital. To this day, we don’t know what happened to him. This really brought home the message that routine life-saving care is beyond the reach of many of our citizens under the current system.”

Helping to coax medical students into primary care medicine is another benefit to the clinic, said Ross, a senior fellow at the Washington University Center for Health Policy. The nation is facing a shortage of primary care physicians — a problem, Ross and other experts say, that is expected to worsen in the coming years for various reasons, including aging doctors planning to retire and a sharp uptick in demand as many people become newly insured under the Affordable Care Act.

Additionally, Ross said, “there is an unfortunate stigma associated with going into family medicine. There’s an improper characterization of the medical student as not being as intellectually focused as the medical student wanting to specialize.”

Primary care doctors also earn significantly less than specialists, an important consideration for
the students who graduate with six figures in medical school debt. Ross cited an annual salary of $150,000 to $200,000 for primary care physicians two years out of residency. By comparison, he said doctors with specialties could command $250,000 to $400,000 a year — and sometimes more — two years out of residency.

Regardless of medical specialty, learning about public health benefits all physicians, Ross said. And teaching it is socially and morally imperative for all medical schools. “It’s a shared responsibility,” he said. “It’s basic humanism.”

Working at the clinic is inspiring second-year students Sagar Mehta and Miriam Ben Abdallah — Saturday clinic board co-chairs and former student coordinators — to seriously consider going into primary care medicine. “You see firsthand that there is a need for primary care physicians,” Mehta said.

On any given Saturday morning, the student coordinators orient all the volunteers, oversee clinic flow and handle any complex patient concerns, research cost-effective medications and, perhaps the most challenging task of all, work the phones to give patients the best referrals for follow-up care. “It is not always easy,” Mehta said. “Resources in St. Louis for the disadvantaged are shrinking.” A case in point was last November’s shuttering of Saint Louis ConnectCare, one of the region’s top providers of outpatient specialized medical care for low-income residents. “You have to think off the top of your head,” Mehta said, “…[and] sometimes you make calls mid-week.”

Many times, the students successfully help patients. Other times, despite ardent efforts, patients’ problems linger or go untreated. This public health reality has taught Ben Abdallah one of the toughest, most important lessons learned during her medical schooling so far: The concept of “healthy packing,” or compartmentalizing distressful emotions to focus on “enthusiasm and optimism” needed to help future patients.

Like most weekends, the line outside of the clinic on the last Saturday morning in September was longer than could be accommodated. Two people were turned away. But that also meant nine people with limited health-care access received help. The clinic was their only option, Ben Abdallah said, adding:

“It’s important to focus on the successes because we want to keep moving forward and help as many people as possible. That is our mission.”
Understanding early childhood depression could alter the course of a life. Sadness, irritability, discouragement & pessimism, decreased enjoyment & motivation, appetite & weight changes, sleep & energy changes, and thoughts of death.

Signs of childhood DEPRESSION

Sadness
Irritability
Discouragement & pessimism
Decreased enjoyment & motivation
Appetite & weight changes
Sleep & energy changes
Thoughts of death

NEARLY ONE IN 10 U.S. ADULTS is clinically depressed.* Of those, approximately one-third have major depressive disorder, a long-lasting and severe form of the illness. It’s a leading cause of disability for people between the ages of 15 and 44. Even when symptoms subside, problems often recur and can periodically disable a person throughout life.

*CENTERS FOR DISEASE CONTROL AND PREVENTION
For many, depression begins in early childhood. That’s one of the major findings from a team of child psychiatrists, psychologists and social workers led by Joan L. Luby, MD, a professor of child psychiatry and director of the School of Medicine’s Early Emotional Development Program. She has spent the better part of her career trying to identify, classify and treat depression in children as young as 3 years of age.

“A primary characteristic of healthy, young preschoolers is that they tend to be inherently joyful,” Luby said. “One of the main symptoms we see in depressed children is anhedonia, which is the inability to experience joy.”

When Luby began her research in the early 1990s, many in the field of child psychiatry didn’t believe preschoolers could be clinically depressed.
Some thought it was possible for children to become depressed only as they got older and started school. Others believed that, even if preschoolers could get depression, it would be impossible to diagnose it so early.

But Luby’s team has demonstrated that both of those opinions were wrong. The researchers found by slightly altering some of the diagnostic criteria to more age-appropriate levels, it was possible to identify and diagnose depression in kids as young as 3. Further, the team discovered that children who are depressed as preschoolers are more likely to battle the disorder when they enter primary and middle schools.

Simply figuring out that some very young children suffer from depression isn’t really the goal, however. Early identification and intervention potentially could alter the course of this often chronic, recurrent disorder. Luby would like to make clinical depression a condition that can be treated and overcome.

“It may be possible to shift the developmental trajectory when children are still young and their brain networks are more plastic and able to change and adapt,” she explained.

Luby and her colleagues are studying an approach known as Parent Child Interaction Therapy-Emotion Development (PCIT-ED), based on a type of therapy developed and tested in the 1970s.

Originally, the technique consisted of two parts. First, the parent was encouraged to get down on the child’s level, play games that the child wanted to play, be very enthusiastic and use effective praising techniques. In the second part, parents learned to use discipline strategies, such as “time-outs,” with their children.

Luby’s team created a third component — the emotion development (ED) part of PCIT-ED. Through this, parents are taught to: recognize their children’s emotions; help their children recognize emotions; and guide their children in effectively regulating these emotions.

A pilot study of the technique showed that depression severity scores decreased by 44 percent in preschoolers during an 18-week intervention. At the study’s end, most of the kids who did PCIT-ED with a parent no longer met the diagnostic criteria for clinical depression.

But that was a small study. Now, the researchers are in the middle of a very large trial of the intervention.

One participant is the 5-year-old daughter of a nurse at St. Louis Children’s Hospital. Requesting anonymity, the mother reported that, after 16 weeks of the PCIT-ED intervention, her daughter is doing much better. Previously, her daughter struggled at home and in preschool. Although the problems have not disappeared, they now are less frequent.
“She has cycles of irritability and tantrums, when she doesn’t like to comply with what’s expected of her,” the mother explained. “When we started the study, she cooperated about one-quarter of the time, but now I’d estimate that she actually does comply the vast majority of the time. And through this type of play therapy, we’ve grown closer because we have to sit down every day and work through things together.”

Additionally, the researchers are using MRI to look at brain structure and function; they want to see whether the brains of depressed preschoolers look and act differently than the brains of young children who are not depressed. Also, they want to learn whether therapy changes anything.

“We’re looking for changes in the way the brain is organizing itself across development,” said Deanna Barch, PhD, the Gregory B. Couch Professor of Psychiatry, professor of psychology and of radiology. “That can be related to changes in the structure of the brain, both in gray matter development and white matter connectivity. It also can be seen in how the brain activates when challenged cognitively or emotionally, as well as the ways that different brain regions communicate with one another.”

The team recently published findings from an imaging study of previously depressed school-age kids in the November issue of JAMA Psychiatry. In 145 children who underwent MRI scans between the ages of 6 and 12, the researchers found that a part of the brain called the anterior insula was smaller in the children with a history of preschool-onset depression. The anterior insula is part of the brain’s insular cortex, which is believed to be involved in emotion, perception, self-awareness and cognitive functioning, among other things.

The anterior insula connects directly with the amygdala, another brain structure closely linked to emotion, and one that functions differently in depressed preschoolers, according to research by Michael S. Gaffrey, PhD, assistant professor of psychiatry.

“It’s too soon to know whether the smaller anterior insula puts children at risk for depression, or whether the condition affects the brain’s anatomy. Studies by other researchers indicate that smaller insula volumes also are common in depressed adults.

First author Andy C. Belden, PhD, said that “pathological guilt,” a key symptom that commonly accompanies depression, is linked with reductions in anterior insula volumes.

Toddlers who display pathological guilt prior to age 3 are 10 times more likely than their peers to be diagnosed with depression by age 5. Guilt, Belden said, may be a strong marker for depression risk.

“Children with pathological guilt tend to apologize, and to genuinely feel bad about very many things, and it interferes with their functioning. The ‘million-dollar question’ is which comes first? Do you have depression and that makes you feel more prone to guilt? Or does a guilt-prone person become depressed?”

To better assess the impact of early intervention, the researchers also are using electroencephalography (EEG) to measure brain electrical activity while study participants view pleasurable scenes. A caplike device worn on the head makes this easier to use in very young subjects.

By comparing those measurements pre- and post-therapy, it is possible to see whether there are any pattern changes in the electrical activity.

“There are lots of reasons to believe that early intervention is going to be much more effective, not only in treating depression, but also across a wide range of brain-related disorders,” Barch said.

Because depression is common, many people don’t view it as being all that serious, Luby acknowledges. This can make it even harder to take seriously diagnoses in young children who are still incapable of fully regulating emotions. But make no mistake, she said, depression is deadly. It is a factor in about two-thirds of the 30,000 suicides committed yearly in the U.S.

“Only depressed people really understand how bad it is,” she explained. “Even people who have serious pain from cancer don’t necessarily want to kill themselves. Depression presents a whole different type of pain, psychic pain, and its depth and severity isn’t fully appreciated in our society.”

Like childhood cancers, Luby suspects depression that begins early in life often may be more aggressive than forms of the disorder that appear later. If PCIT-ED, or some other therapy, can change the path of the illness, a good deal of disability, psychic pain and even death may be prevented.
Windows into Ancient Lives

Three distinguished St. Louis residents arrive for checkups:

**Pet-Menekh**
4th–3rd Century BC

Linen packs, probably containing organs, were found inside the body. Tissues were permeated with resin, a preservative for mummification.

**Henut-Wedjebu**
1391–1350 BC

Female wearing a headdress, her brain and lungs uncharacteristically intact. Apparent calcium deposits, circled, suggest possible tuberculosis.

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*18 Washington University School of Medicine*
Three distinguished St. Louis residents arrive for checkups, offering enduring lessons in art, science and humanity.

Amen-Nestawy Nakht
4TH–3RD CENTURY BC

Linen packs, probably containing organs, were found inside the body, coated with resin, a preservative for mummification.

An unfortunate grave robbery desecrated the body. But hidden away near the heart is a scarab amulet placed in hope of rebirth.

Ancient Lives, offering enduring lessons in art, science and humanity. 

BY MICHAEL C. PURDY
The School of Medicine recently teamed up with the Saint Louis Art Museum and Washington University’s Mildred Lane Kemper Art Museum to scan some very unusual patients: three Egyptian mummies.

One of the mummies, Amen-Nestawy-Nakht, a 3,000-year-old Egyptian priest, is owned by the Saint Louis Art Museum. The other two mummies — Pet-Menekh, a priest from the 3rd or 4th century, BC, and Henut-Wedjebu, a female from the 13th century — belong to Kemper Art Museum but are on long-term loan to the Saint Louis Art Museum.

The Saint Louis Art Museum is preparing for a reinstallation of the mummies, and curators there thought computerized tomography (CT) scans might provide information about the mummies and their societies.

Art movers carefully transported the mummies across Forest Park to the Center for Advanced Medicine, where they were scanned one by one.

Among the early findings: One of the mummies, the female, already was known to have a brain, but scans revealed she also still has lungs. Typically, the brain and lungs were removed before burial.

Radiologists with the university’s Mallinckrodt Institute of Radiology discovered that the same mummy also has an array of small objects around her head. She appears to be wearing a headdress or embellished shroud, but it’s also possible that she is surrounded by packing material or debris.

The scientists were surprised to find that a second mummy appeared to be significantly shorter than his sarcophagus. Further scanning revealed that his head had been dislodged from his body, perhaps when grave robbers ransacked his tomb. They found an item on his chest that may have been a burial amulet missed by grave robbers. They are using the scanning data to reconstruct the item with a 3-D printer.

Mummies are incredible time capsules from human societies that vanished thousands of years ago. Opening their capsules, however, would desecrate the human remains and possibly destroy unique cultural treasures. Modern medical imaging techniques offer ways to peer into these time capsules without physically opening them.

Scientists scanned Amen-Nestawy-Nakht two decades ago, but imaging technology has advanced significantly since then.

For the new study, a team of School of Medicine and hospital volunteers used a powerful and recently installed CT scanner. The unit uses X-rays to virtually slice a solid object, producing detailed 3-D images of its interior.

The logistics of getting the mummies from the art museum to Washington University Medical Center and into the scanners were very complicated, acknowledged Sanjeev Bhalla, MD, professor of radiology and chief of cardiothoracic imaging. But, Bhalla said, another aspect of the project was just as challenging: “It was very important for us to remember that these were human beings we were scanning.”

Bhalla said the project was a team-building exercise, an opportunity for people from many disciplines to collaborate together. “We had to do the scanning in an atmosphere of spiritual and physical respect and, with the help of museum staff who acted as a kind of surrogate family for the mummies, we did that,” he said.

Additional findings are forthcoming.

“It was very important for us to remember that these were human beings we were scanning.”

SANJEEV BHALLA, MD

Examining Pet-Menekh’s mummy, from left, are curators Lisa Çakmak, PhD, of Saint Louis Art Museum, Karen Butler, PhD, of Kemper Art Museum, and School of Medicine radiologists Sanjeev Bhalla, MD, and Vincent Mellnick, MD.
THE BEST Defense

Vigilance, research and response to the threat of infectious disease

BY DEB PARKER AND RICK SKWIOT
HUMANS ARE LIVING IN UNPRECEDENTED TIMES

as multiple infectious diseases threaten to become public health issues. Ebola is grabbing headlines, but other important risks, such as Chikungunya and Enterovirus D-68, also have the potential to become the next big story.

“And, like death and taxes, there is always the flu,” said Steven J. Lawrence, MD, MSc, who works with health departments to prepare for, identify and respond to communicable, large-scale public threats. “We don’t know how bad it will be, or what ages will be most affected each year, but we know it will be there.”

New and re-emerging infectious diseases pose a constant challenge. But whatever the threat, a network of physicians, researchers and other health-care professionals at Washington University Medical Center works determinedly to keep our community and the world safe from infectious diseases.

Preventing the next epidemic requires effort on many fronts: monitoring emerging diseases, conducting basic scientific research, training caregivers in specific patient-care protocols and advising public health officials on the appropriate response to outbreaks.

Scientists here are working to understand how viruses attack the body and evade the immune system and, ultimately, how to disable them. The Genome Institute at Washington University, one of only three National Institutes of Health (NIH)-funded, large-scale DNA sequencing centers in the U.S., frequently collaborates with researchers and physicians to pinpoint critical variations in pathogens, knowledge that can lay the foundation for disease treatments and discoveries.
Many diseases — from anthrax to plague — begin in animals. As people encroach on previously uninhabited spaces, there are more interactions with animals. Dozens, if not hundreds, of these naturally occurring infections in animals have yet to take root in humans, said Lawrence, an assistant professor of medicine in the Division of Infectious Diseases.

A case in point: The SARS coronavirus. This viral respiratory disease, recognized for the first time in humans in early 2003, originated in bats. The bats infected animals that later were sold for food in live markets in Guangdong Province, China. The disease spread to 29 countries — expedited through global airline travel — resulting in more than 8,000 cases and 776 fatalities.

Spearheaded by the World Health Organization, the international community responded with unheard-of speed, putting aside scientific rivalries and sharing data for the common good. Because of this, global data sharing is much more forthcoming today.

Washington University’s David Wang, PhD, then a postdoctoral student and now an associate professor of molecular microbiology and of pathology and immunology, gained international prominence when he and a small group of researchers used a new technology — a pan-viral microarray assay — to identify the novel SARS virus in 2003. Wang’s Pathogen Discovery and Infectious Disease Genomics Lab is a global player in identifying the guilty viral agent in disease outbreaks via advanced investigative technologies.

Amazingly, SARS has been eliminated in humans, purely through diagnostic testing and infection control, without the help of a vaccine or antiviral drug. Since the outbreak ended, there have been no new cases. “SARS had an almost 10 percent case fatality rate, and it was probably airborne in some instances,” Lawrence said. “It was really, really scary. Its elimination was a magnificent public health triumph.”

In the early stages of an outbreak, physicians or public health officials often see something a little crazy, or outside the norm — a cluster of illnesses that test negative for the usual offenders.

In Queens, New York, in 1999, an astute doctor realized it was unusual for two cases of encephalitis to occur in a small neighborhood. Simultaneously, thousands of crows were dying in the city. West Nile Virus had just established itself in North America.

Early cases may go unnoticed until people start putting the puzzle together. Through tools such as ProMed-mail, an internet reporting system of the International Society for Infectious Diseases, physicians can log unusual symptoms. Dedicated to the rapid dissemination of information, the site includes official reports and accounts from media and local observers.

Washington University doctors closely follow the global situation and work hand in hand with the Centers for Disease Control and regional, state and local public health officials.

State laws require that health-care providers and laboratories report some types of infectious diseases to local health officials. St. Louis City Health Director Pamela Walker, MPH, regularly monitors results of statewide lab tests.
The health department follows up on all local reported disease cases, making sure infected people are receiving appropriate care and also tracing recent contacts to curb the spread. Guidance from Washington University doctors, Walker said, is critical in this process.

On a weekly basis, Walker seeks support from School of Medicine doctors on everything from sexually transmitted diseases to tuberculosis to health disparity issues. “I couldn’t possibly afford to pay for that level of expertise,” Walker said. “All of these physicians donate their time. The generosity is amazing. They just do it because they care.”

Lawrence, an epidemiologist, can explain infectious disease recognition and risk in terms that are easily understood, or rabbit fever. This was a natural occurrence, not an act of terrorism. School of Medicine doctors helped health departments come up with good surveillance plans so that hospitals could identify and deal with cases of tularemia if any occurred.

Recognition is the important first step in containing any infectious disease threat, Lawrence said. “Once you recognize the illness, you can begin to determine the extent of it,” he said. “How many cases? Is it spread by direct contact? You can’t control it until you know how it is spread. The more you know about how a bug works, the more you can do to minimize the risk. You have to look at who’s gotten sick and who hasn’t. What are the risk factors?”

In the 1976 and 1995 Ebola outbreaks in the Democratic Republic of the Congo, it became clear that three groups were at a much higher risk: those who took care of an Ebola patient in their household or in a hospital and those involved in burial of Ebola patients. These same risk factors are playing out in today’s Ebola crisis.

While the population remains increasingly vulnerable to infectious diseases, technology is light-years ahead of where it was even 10 years ago. “A lot of this has to do with diagnostic testing and the ability to sequence new pathogens very quickly,” Lawrence said. “This in turn leads to the capacity to come up with possible treatments or vaccines much faster than in the past.”

RESEARCH SPECTRUM The program of investigation ranges from basic science inquiry to sequencing work at The Genome Institute.

Walker said. Recently, he created a training video on Ebola, MERS (Middle East Respiratory Syndrome), Chikungunya and Enterovirus D-68 for health and human services staff, EMS workers and airport staff that every county in the region now uses.

As another means of surveillance, sensors in St. Louis can detect the release of deadly pathogens in the air in a terrorist attack. These sensors, also positioned in other major U.S. cities, are part of Homeland Security’s BioWatch program. Lawrence, who serves on the regional advisory committee for BioWatch, describes the sensors’ locations as “very sensitive information,” which terrorists could try to sabotage.

In October 2006, BioWatch sensors near Busch Stadium in downtown St. Louis received a positive signal for tularemia, or rabbit fever. This was a natural occurrence, not an act of terrorism. School of Medicine doctors helped health departments come up with good surveillance plans so that hospitals could identify and deal with cases of tularemia if any occurred.

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In the Kansas City area last year, doctors began seeing severe respiratory illness in young children, with some requiring hospitalization or a ventilator. Nationwide, the virus, identified as Enterovirus D-68, spread rapidly; in rare cases, it has caused paralysis and death.

In collaboration with Greg Storch, MD, The Genome Institute recently sequenced the genome of Enterovirus D-68, sampled from patients treated at St. Louis Children’s Hospital. Kristine Wylie, PhD, research instructor in pediatrics, and Todd Wylie, director of microbial genomics computing, also were key members of the team. The results were immediately fed into the NIH genetic sequence database, GenBank, enabling access by scientists worldwide.
Storch, the Ruth L. Siteman Professor of Pediatrics, said the genetic data could be used to quickly develop a more reliable diagnostic test for the virus, so doctors will be able to confirm whether a child has the disease. There is no treatment and no vaccine, but having the DNA sequence available is a major step toward both goals.

Similarly, in October 2011, the St. Louis County Department of Health identified a cluster of E. coli-infected patients who had consumed salad bar items at supermarket chain stores. The outbreak sickened several dozen people in the Midwest, but not all cases had exposure to the suspected source.

Some questions could not be answered via lab methods routinely used in such investigations. Missouri State Epidemiologist George Turabelidze, MD, called in renowned expert on the bacterium, Phil Tarr, MD, the Melvin E. Carnahan Professor in Pediatrics and head of pediatric gastroenterology, who suggested using the resources of The Genome Institute. This marked the first time whole genome sequencing methodology was used for an E. coli outbreak investigation.

“Out of a couple million base pairs we found one or two nucleotide differences that sorted out epidemiologically perfectly,” Tarr said. “It validated the use of this technology to bring molecular clarity to outbreaks and focus public health resources. This work shows how powerful this technology can be. Now other people can build on these findings.”

The resulting study published by Tarr, Turabelidze and colleagues in the School of Medicine and at Washington State Public Health Laboratories, helped push the CDC to further speed up development of new technologies for outbreak investigations, Turabelidze said.

Despite these advances, Lawrence said, time-tested medical knowhow — contact tracing, hand hygiene and seasonal flu shots — can work wonders in stopping the spread of disease.

“It’s the simple things we’ve always known since John Snow (considered the father of epidemiology) traced a cholera outbreak to a water pump handle in 1854,” he said.

Unfortunately, previously controlled diseases are making a comeback due to lower vaccine compliance. The scientific community has done such a good job controlling diseases — most people today have never seen a case of polio, for instance — that many have become complacent.

Public concern is more focused on Ebola, but the chance of an uncontrolled Ebola outbreak in the U.S. is next to zero, Lawrence said. The disease is not easily transmitted, except in severely ill patients, and an advanced health-care infrastructure can effectively contain it.

“Old technology, basic infection control and isolation, stopped SARS,” he said. “It can also stop Ebola, even in the absence of widely available antiviral drugs to work against it.” While any case is tragic, Lawrence said, it’s important to note that of the more than 1,000 direct interactions between health-care workers and the nine Ebola patients on U.S. soil, there were two instances of transmission, as of December 2014.

“We can take care of an infection we’ve never seen in the U.S. before. We have a history of a strong infectious disease infrastructure to rapidly identify and put suspected patients in the right setting with the right kind of care — at Washington University Medical Center and in many U.S. hospitals,” Lawrence said. “The threats are always different, but there are always ways to defend against them.”

PREVENTION To protect patients and themselves, School of Medicine employees now must receive flu vaccinations per a 2013 policy change. Barnes-Jewish Hospital health-care professionals provide free flu shots to tens of thousands of St. Louisans annually.
On the SPOT care
Youth clinic heads to school in north St. Louis County

A one-stop, drop-in clinic offering free confidential medical care, mental health counseling, testing for sexually transmitted diseases (STDs) and HIV, and other services to youth aged 13 to 24: That’s the mission of The SPOT (Supporting Positive Opportunities for Teens). Located in St. Louis City, this Washington University clinic has had a huge impact, treating more than 10,000 since opening in 2008.

The SPOT Medical Director Katie Plax, MD, director of adolescent medicine and professor of pediatrics, noticed that many SPOT patients came from the north St. Louis County municipalities of Ferguson, Florissant and Jennings.

“The majority of St. Louis County youth we see are from north St. Louis County,” said Plax. “We wanted to figure out something that would be convenient and closer to them.”

At the same time, Jennings Senior High School Principal Dayle Burgdorf was looking for ways to keep kids at school. Burgdorf learned that the long treks some students must make to take care of chronic health conditions are a major cause of absenteeism. She then met with Sarah Garwood, MD, an assistant professor of pediatrics and physician at The SPOT, to discuss the problem, and the idea for a school-based health clinic was born.
“The idea of bringing the clinic to the kids is very appealing to us,” Burgdorf said.

The Jennings School District is modifying a room to house the clinic, and funding from the St. Louis County Children’s Services Fund supports this collaborative effort. The new school-based program will offer mental health counseling, case management and wellness education. The team hopes to provide medical services in the near future, but at this time funding to provide medical care has not yet been achieved.

“This is an opportunity to make health-care services accessible for students and families,” said Anthony Robinson, EDD, director of secondary education at Jennings Senior High School. “It helps build healthy communities and, in turn, helps students with academic performance.”

While only Jennings High School students will be able to use the clinic, Garwood, Plax and The SPOT Program Director Kim Donica, LCSW, view this as a starting point to open similar clinics in other north St. Louis County schools.

The city-based SPOT

When The SPOT opened its doors at its first location (4169 Laclede Ave.), organizers expected to serve 500 youth in the first year. Instead, clinicians served that many in three months. In 2009, The SPOT’s first full year of operation, 1,879 new patients sought assistance.

“The numbers have steadily increased each year,” Donica said. “We’re on track to serve more than 3,000 clients in 2014.”

SPOT medical staff members are affiliated with Washington University, and the clinic also partners with community-based organizations to provide many services under one roof. For example, The National Council on Alcohol and Drug Abuse supplies a full-time substance abuse counselor at The SPOT.

The clinic offers shower and laundry facilities and a recreational space where youth can watch TV, surf the Internet, grab a snack or participate in counselor-led activities.

Plax said the “safe drop-in space” is key to The SPOT’s success. “Youth can come check us out, see what the place is like, and engage in any of the other services we offer,” she said. “Meeting The SPOT staff helps them overcome the stigma of seeking help.”
Delivering when it counts

Although there are many reasons for The SPOT’s success, one thing is certain: Young adults need support to become successful adults. “This is a critical juncture to learn the skills to be a healthy and functional adult,” Plax said. “Times are hard, youth unemployment is high, and people need help and support to launch.”

Plax and Donica see many opportunities to help more youth. One priority is to attain funding for basic medical care for older youth. The SPOT is temporarily funded by grants, some of which are not renewable. Many patients are 20 to 24 years old — too old to qualify for state and local government funding.

“Federal grants by and large don’t cover medical care because there is the belief that it is going to be covered by Medicaid expansion,” Donica explained. Missouri opted out of Medicaid expansion and, as a result, many youth are in a coverage gap and lack health insurance.

Additionally, The SPOT needs increased nursing and medical support. One full-time nurse sees more than 25 patients per afternoon, along with an adolescent medicine physician. A psychiatrist and a gynecologist come once a week, not often enough to meet the demand.

Cramped facilities also present problems. The SPOT is housed in 2,500 square feet, with just two exam rooms.

“We’re at capacity here,” Plax said. “We just can’t fit any more people in this space.”

Despite some of the limitations, youth see The SPOT as a sanctuary. “I probably wouldn’t be alive if it weren’t for the people here,” said Alexis, 22.

After leaving her family home in anger, Alexis caught a ride with a friend to St. Louis. She learned about The SPOT while at a homeless shelter for teens.

SPOT staff helped her find housing, job training and employment during the three years she lived in St. Louis. Alexis now has two jobs, one as a pharmacy technician and one as a customer service representative — and she is enrolled in college.

Alexis credits The SPOT staff for helping to reunite her with family members. She moved back home six months ago.

While the school clinic will have a slightly different focus, both clinics will operate from the same set of core principles: creating community partnerships, involving the medical science community to optimize care, and taking action to improve health-care delivery for kids.

But the SPOT’s mission goes beyond medicine. “I don’t think medical people speak about it enough but really this is about love,” Plax said.

“You do this work because it comes from your heart. And you do this kind of engagement because you have a deep appreciation for that person sitting before you.”

To learn how you can partner in this important endeavor, call 314-935-9691.

The smell of fresh-baked cookies, fun games to play and creative projects make the current SPOT an inviting place, one that goes above and beyond in its sensitive health-care mission.

“I probably wouldn’t be alive if it weren’t for the people here.”

— ALEXIS —
Transformative creativity

Inspirational grandpa made a lasting impression, one that will benefit others

While undergoing cancer treatment, George Holway was determined to keep playing with his grandkids.

“When the grandchildren would come to visit, they got to fingerpaint with him,” said his wife of 40 years, Diana Holway. “He couldn’t run around with them, so I’d put art supplies on the floor and there they’d go!”

It’s no wonder that George’s grandchildren remember him, even those who were very young when he died in 2012.

Ten years earlier, George had been diagnosed with multiple myeloma. In this type of cancer, abnormal white blood cells build up in bone marrow, forming tumors and preventing the bone marrow from making healthy blood cells.

Just as he had found a creative way to play with his grandchildren, George was open-minded about treatment. Under the care of Ravi Vij, MD, associate professor of medicine in oncology at Washington University, he participated in genetics studies and clinical trials for drugs that later received FDA approval.

At the time, multiple myeloma had a five-year survival rate.

“If it wasn’t for Siteman Cancer Center and for Dr. Vij’s team, he wouldn’t have lived as long as he did,” Diana said.

The couple was so impressed with the team at Washington University that they made gifts toward multiple myeloma and breast cancer research. After George’s death, Diana and her children — Susan Maher, Lindsey Smith and Paul Holway — made another gift.

“The Holway gifts were transformative, helping us initiate many multiple myeloma studies and identify mutations that contribute to the disease,” said John F. DiPersio, MD, PhD, chief of the Division of Oncology and deputy director of the Alvin J. Siteman Cancer Center at Barnes-Jewish Hospital and Washington University School of Medicine.

The pilot research led to three successfully funded National Institutes of Health (NIH) grants, one Department of Defense grant, and grants from organizations such as the Multiple Myeloma Research Foundation.

Michael Tomasson, MD, associate professor of medicine, is focused on understanding the disease’s mechanisms.

“We know there is a pre-malignant phase of myeloma, which can be detected with a blood test,” he said. “If we could figure out who is going to get multiple myeloma and interfere with that process, we could catch myeloma early.”

In the past few years, Washington University has been recognized nationally for its role in advancing research and accelerating the approval of multiple myeloma drugs.

“We’re now among the top half-dozen respected centers in terms of myeloma research, spanning the spectrum from basic science to translational to clinical,” Vij said.
Honoring a fierce champion

Everyone who has worked closely with Philip W. Majerus, MD, professor emeritus of medicine in hematology, has stories. Students recall the hours he spent with them, doing experiments and going over data, and the many heated discussions in which Majerus challenged them to look critically at their research. Those trainees who proved their mettle gained his fiercest loyalty.

On Sept. 19, following announcement of Majerus’s retirement from research (he will continue to teach), more than 100 former trainees worldwide attended a symposium in his honor. A member of the National Academy of Sciences, Majerus is renowned in the scientific community for, among other things, discovering how aspirin prevents blood clots. This particular finding led to millions of people taking “baby aspirin” daily to prevent heart attacks.

Creating a Fellowship

Former trainees remember something else: a passionately dedicated teacher who inspired them to go beyond what they thought was possible. As a tribute, they have created the Philip W. Majerus Endowed Fellowship in Hematology.

“They say in academia that if you train one or more people to go on and do what you do, then you had an outstanding career,” said John D. York, PhD, the Natalie Overall Warren Professor and Chair of Biochemistry at Vanderbilt University. “Phil has trained 50 to 100 people who have gone on to become professors or physician-scientists who do what he does.”

“He really spent a remarkable amount of time with each person,” said Sandra Hofmann, MD,
PhD, professor of medicine at the University of Texas Southwestern Medical Center. “He liked to sit down with students and look at the primary data in a great amount of detail. He had a really good instinct for uncovering where there might be holes in data.”

As Majerus explains: “To me, there are basically two kinds of laboratories. There is a results-getting laboratory, and there is a training laboratory, and they’re not the same.

“If you have a results lab, you get technicians to do all the background work, and the postdoc just does the critical experiments. In a training lab, the trainee has to start from scratch and do all the grunt work. In doing so, the trainee learns to function independently.”

“...if you did persuade him that you were right, he became your staunchest champion and would give you the credit.” — Joe Miletich, MD, PhD

Joe Miletich, MD, PhD, senior vice president of discovery research, preclinical sciences, and early development at Merck, remembers Majerus’s abrasive style as a rite of passage.

“He was really critical about what you presented as data or facts or conclusions,” Miletich said. “And he would push almost in an aggressive way sometimes. But, if you did persuade him that you were right, he became your staunchest champion and would give you the credit.”

To help students become more established, Majerus generously shared his network of contacts.

“Phil was fiercely engaged in his trainees’ career development,” York said. “He really cared about the success of his people.”

Miletich, Hofmann and York said that training with Majerus transformed their careers. Today, they still use his rigorous approach.

A storied CAREER

Majerus earned a medical degree from Washington University in 1961 and completed post-graduate training at Massachusetts General Hospital and the National Heart Institute in Bethesda, Maryland. In 1966, he joined Washington University as an assistant professor of biochemistry. For most of his tenure, he has held leadership positions — serving as co-director of the Division of Hematology and Oncology from 1973 to 1994 and continuing as co-director of the Division of Hematology from 1994 to 2009.

Evan Sadler, MD, PhD, chief of the hematology division and professor of medicine in hematology, said an endowed fellowship supporting young scientists is a fitting tribute to Majerus. “That makes sense, given his long track record of training future scientists,” he said.

More than 34 former trainees contributed to the fellowship, which reached the endowment threshold of $100,000 in just one month and $300,000 by the symposium date, and it continues to grow.

This is the first named fellowship in hematology, signaling a new direction for Washington University at a time when fewer funds are available to train young scientists, said Victoria Fraser, MD, PhD, the Adolphus Busch Professor and chair of the Department of Medicine.

“Having institutionally based fellowships to support really promising young scientists is extraordinarily important,” she said.

For Miletich, honoring someone who influenced him so dramatically serves a dual purpose: showing appreciation and “reloading for the future.”

“There will be new kinds of Phils that come along,” he said. “You want to make sure there’s a steady supply of them. Because the world’s better off if there is.”
Dual legacy
Family supports students and completes a life’s work

Occupational therapy was a great love of the late Pauline Cid Schultz’s life, according to her children. After graduating from the Program in Occupational Therapy in 1944, she spent many decades working in the field. In her estate, she provided for the Pauline Cid Schultz Occupational Therapy Scholarship to make it possible for others to enter the profession.

Family members — son Gordon Burkhart-Schultz, his wife, Karolyn, and his sister, Korine — later visited the School of Medicine to formally establish the scholarship. At the time, Schultz’s children had no idea they would find a home for their father’s life work as well.

Carolyn Baum, PhD, the Elias Michael Executive Director and professor of OT, neurology and social work, had planned an entire day of presentations and activities to thank the family for its support. Baum and other researchers spoke on the occupational therapy program’s initiatives and its collaborative, multidisciplinary approach. That’s when Burkhart-Schultz realized how perfectly the program’s methodology fit with the still unfinished work of his late father, psychologist Karl V. Schultz, PhD.

“We were in the conference room and Gordon asked if we could talk in the hall,” Baum said.

Burkhart-Schultz also remembers the moment: “How everything just came together was, to me, actually astonishing.”

By chance, Burkhart-Schultz had a copy of a values-based personality test his father had been developing for decades.

“Developing this instrument was one of the most important things in dad’s life, and it would dominate many conversations,” Burkhart-Schultz said.

Karl Schultz died in 2006, but had left money in his estate to validate and complete the test, which measures how a person views activities in terms of importance and satisfaction. Schultz’s idea was that people ascribe importance to activities that do not truly satisfy them, which is how they end up in professions that make them unhappy.

“We showed my father’s work to Carolyn and her immediate take, within two minutes, was ‘This is totally unique,’” Burkart-Schultz said.

Years earlier, Baum had developed a different assessment test — the Activity Card Sort (ACS) — now used by OTs worldwide to evaluate daily living activities. Combining the ACS with the Schultz Lifestyle Series might help OTs understand not just behavior but also motivation, Baum said. This depth of understanding would aid OTs in designing individualized programs and setting treatment goals.

Baum and former faculty member Lisa Connor, PhD, MSOT, now inaugural chair and professor of OT at Massachusetts General Hospital Institute of Health, presented “The Schultz Lifestyle Profile Series Instrument: Psychometric Properties and Relationship with Activity Participation” at the 16th International Congress of the World Federation of Occupational Therapists in June 2014. They are preparing to publish a paper.

Burkhart-Schultz is thrilled. “Having the fulfillment of my dad’s lifelong work converge with the love and passion of my mother’s life, in the way that it did, is quite special,” he said.
### 1950s

**Galen B. Cook, LA 51, MD 55**, became a published author of nonscientific material with the release of his new book, “Wild Cards,” a parody on business cards that uses the real names of real people (e.g., attorneys-at-law Dewey, Cheatham & Howe).

### 1960s

**John Crane, MD 64**, closed his private practice of 38 years and now works part time as a staff psychiatrist at the Catholic Family Services clinic in Union, Mo. He is a Distinguished Life Fellow of the American Psychiatric Association. In his free time, Crane enjoys sailing, writing, painting, wood sculpture and traveling with his wife and their labrador retriever in their motor home.

**Warren Howe, MD 65**, retired from active practice in 2011. He was appointed by the governor to Washington State’s Medical Quality Assurance Commission. He continues to volunteer with local high schools’ sports medicine activities and the Washington Interscholastic Activities Association. He and his wife, Hedy, enjoy their two grandchildren and traveling.

### 1970s

**Michael Finkel, MD 73**, retired from clinical practice in May 2014. During his career, he treated patients in private multi-specialty groups and as a staff member of the Mayo Clinic and the Cleveland Clinic. He served as president of the neurology state societies in Wisconsin and Florida, as an active member of the American Academy of Neurology, and participated in the World Federation of Neurology and the World Neurology Foundation. Finkel is looking forward to volunteering at the Naples Botanical Garden and as a reading tutor at Fun Times Nursery School in Naples, Fla.

**Robert Weiss, MD 74**, is finishing a year of service with the Peace Corps and SEED Global Health in Uganda. His mission includes strengthening and creating teaching programs in the various Ugandan medical schools. Weiss primarily has taught third- and fifth-year medical students at Mbarara University of Science and Technology and also served as a consultant to the hospital interns and pediatric residents (house staff).

### 1980s

**W. Patrick Davey, MD 81**, was appointed vice chair of the accreditation committee for the Accreditation Association for Ambulatory Health Care (AAAHC) Board of Directors, representing the American Academy of Dermatology. AAAHC is a national organization that accredits a variety of health-care organizations and signifies dedication to quality patient care.

**Keith Churchwell, MD 87**, was named to the American Heart Association’s Greater Southeast Affiliate Board of Directors for the 2013-14 fiscal year. He is associate professor of medicine and radiology, director of cardiac imaging, and executive director and chief medical officer for Vanderbilt Heart and Vascular Institute in Nashville.

### 1990s

**Steven Harvey, LA 88, MD 92, HS 96**, recently formed Premier Psych TMS St. Louis, a company that provides transcranial magnetic stimulation (TMS) treatment for depression and other conditions. It is the only TMS installation in the St. Louis metro area to use the newer FDA-approved TMS machines. He and his wife, Chantelle (Schmidt) Harvey, EN 88, GR 97, have two daughters, ages 10 and 15.

**Jennifer Sambrook Pitonyak, OT 97**, defended her dissertation, “The Contexts of Life Course Health Development Associated With Exclusive Breastfeeding in the United States,” and graduated with a PhD in health policy in May 2013. She is vice chair and assistant professor in the Department of Occupational Therapy at the University of the Sciences in Philadelphia.

### 2000s

**Jonathan Chung, MD 04**, is associate professor, director of Radiology Professional Quality Assurance and director of the Cardiopulmonary Imaging Fellowship at National Jewish Health in Denver. In December 2013, he received the Honored Educator Award for delivery of high-quality educational content to the Radiological Society of North America.

**Kevin Wilson, MD 05**, completed an otolaryngology residency at the University of Michigan and took an academic job at the University of Utah. He and his wife, Emily, have four children and enjoy living in Utah.

**William McCoy IV, MD 13, GM 13**, received IRB approval on his first project, is starting post-medical school research and is actively recruiting study participants. He is in a preliminary year internship, with a specialty in dermatology, at Barnes-Jewish Hospital.

### In Memory

**Milenda Arcelona, HS 60**

Arcelona died Wednesday, Jan. 8, 2014. She was 84. Born in the Philippines, she graduated from Far Eastern University with a medical degree in 1958. After an internship at Lutheran Medical Center and residency at Barnes Hospital, she returned to the Philippines as a private practitioner in pediatric medicine. Arcelona returned to St. Louis with her family in 1973 and managed her husband’s medical practice. She was active in cultural and medical communities, including the Philippine Medical Association, the Filipino-American Society and the Association of Practicing Physicians in America.

**John R. Calvert, MD 58**

Calvert died Saturday, June 28, 2014. He was 82. A native of Natchez, Miss., he attended Washington & Lee University in Virginia and, later, Washington University
School of Medicine. He practiced anesthesiology in Atlanta for 40 years at the Emory University Hospitals and School of Medicine and Atlanta Outpatient Surgery Center. After retirement, Calvert moved to Prescott, Ariz. He enjoyed caring for his family, gardening, studying geology, traveling, being active at church and other volunteer opportunities.

Patricia “Patsy” Condit, PT 59
Condit died Thursday, May 15, 2014. She was 76. A longtime resident of Texas, Condit was a proud member of First Presbyterian Church in Seminole, Texas, and later Cibolo Creek Community Church in Fair Oaks Ranch. She devoted much time and energy to her church, but also was very proud to be a mother and, later, “Mamaw” to her grandchildren. She is remembered fondly by her friends and family and for her generosity to others.

David S. Johnson, MD 48
Johnson died Saturday, April 12, 2014. He was 89. Johnson, who grew up in Jerseyville, Ill., initially enrolled at Washington University as a pre-med student, but was sent to Miami University to continue his pre-med requirements after registering in the U.S. Navy’s V-12 college training program on his 18th birthday. He returned to Washington University as a medical student and graduated in 1948 with a medical degree. Johnson joined the U.S. Army during the Korean War and afterward completed a residency at Duke University. Johnson eventually moved to Portland, Ore., where he became chief of pathology at Good Samaritan Hospital until his retirement in 1990. Johnson enjoyed golf, reading historical biographies, learning about Civil War history and spending time with family.

Edwin Dominic Kadlub, MD 48
Kadlub died Sunday, April 27, 2014. He was 91. After joining the U.S. Army in 1943, Kadlub focused on pre-med studies at Stanford University and then enrolled at Washington University School of Medicine. He opened his first practice in Dove Creek, Colo., in 1950, but returned to the Army in 1953 and served in Korea and Okinawa. He was discharged from duties in 1955 and moved to Windsor, Colo., where he practiced medicine until 1988. As a physician he was known for his patient care and bedside manner, making house calls at all hours and even seeing patients without appointments. Kadlub was president and member of numerous professional, civic and church-related boards and organizations. He and his wife, Marjorie, were selected as Citizens of the Year by the Windsor Chamber. His additional hobbies included woodworking, reading, singing and travel.

Lindell Cook Owensby, MD 44
Owensby died Sunday, Jan. 19, 2014. He was 92. He graduated from Manhattan High School, attended Kansas State University and graduated from Washington University School of Medicine. He was a proud U.S. Army veteran, having served in active duty from 1941-44 and inactive duty from 1944-47. Owensby was an assistant resident in ophthalmology at Barnes, St. Louis Jewish and St. Louis Children’s hospitals. He was a staff doctor and, eventually, an assistant medical director at the State Sanatorium for Tuberculosis in Norton, Kan. In 1953, Owensby began private practice in Concordia, Kan., and retired in 1988. He became a diplomat of the American Board of Ophthalmology in 1954. Among his other interests were reading, sailing, playing golf, amateur radio and making beer and wine.

Russell Dallmeyer Shelden, MD 49
Shelden died Friday, June 20, 2014. He was 92. A lifelong resident of Kansas City, Mo., Shelden earned degrees from the University of Missouri-Columbia (Mizzou) before attending Washington University for his medical education. He completed an internship at Kansas City General Hospital and residency at Research Hospital where he practiced anesthesiology until his retirement. Additionally, Shelden served as a member of the U.S. Army Reserves for 52 years, attaining the rank of colonel, and received military honors, including three battle stars from World War II. He served as president of the Kansas City Society of Anesthesiologists and the Missouri Society of Anesthesiologists, and as a member of the board of directors of the American Society of Anesthesiologists. He and his wife, Mary, created the Russell D. and Mary B. Shelden Professorship in Anesthesiology in 1998 at Washington University. The couple also supported many philanthropic efforts at Mizzou and in their community. In appreciation for their dedication to Washington University, they received the Robert S. Brookings award in 2006.

S. Michael Freiman, MD 55
Freiman died Thursday, July 17, 2014. He was 85. Born to Polish immigrants in New Jersey, Freiman attended the University of Montana and Washington University School of Medicine. Following graduation in 1955, he served a tour in the U.S. Navy before returning to St. Louis for gynecology training. During his residency at Barnes Hospital, Freiman became a fellow of the late William Masters, MD, and headed the infertility clinic. He closely followed women’s rights and access to safe care during his career and performed the first legal abortion in Missouri after Roe v. Wade in 1973. He treated women at Reproductive Health Services from 1978-1986. In 2000, the St. Louis Women’s Political Caucus awarded Freiman the “Good Guy” award in recognition of his contributions to women’s reproductive health. He also was a women’s health consultant for the American Heart Association and the Agency on Aging with Developmental Disabilities. Freiman was a clinical assistant professor in the Department of Obstetrics and Gynecology at Washington University, where he helped start the cytogenetics lab.
Louis Gilula, MD
Gilula, a faculty member for more than 30 years, died July 2, 2014. He was 71. A founder and longtime leader of the musculoskeletal section at the school’s Mallinckrodt Institute of Radiology (MIR), Gilula was a professor of radiology, orthopaedics and plastic and reconstructive surgery when he retired in October 2013. Gilula was known internationally for his expertise in wrist imaging, and he authored one of the major texts on this subject. He was also a pioneer in pain management, offering patients therapeutic spine injections before they became commonplace. A native of Lubbock, Texas, Gilula earned a medical degree at the University of Illinois School of Medicine in 1967. After internships and residencies at San Francisco General Hospital, Dewitt Army Hospital in Fort Belvoir, Va., and Max C. Starkloff Memorial Hospital in St. Louis, he became a radiology instructor at Washington University School of Medicine in 1973.

Mary Langston Parker, MD 53
Parker, who made an indelible mark at Washington University, first as a dedicated, tireless physician and researcher and then as the university’s director of student health services, died Saturday, May 24, 2014. She was 89. She was an associate professor emeritus of preventive medicine and a mother of five. Parker’s death came nearly 13 months after the death of her husband of 59 years, Charles Ward Parker, an emeritus professor of medicine. A Florida native, Parker earned a bachelor’s degree in 1946 from Florida State College for Women and a master’s degree in 1949 from Florida State University. In 1949, Parker enrolled at WUSM as one of seven women in her class and later graduated cum laude. She first worked in the university’s Student Health Services, but then became involved in endocrinology research, helping develop a blood test for human growth hormone. In 1968, Parker decided to focus more on patient care and returned to Student Health Services. She was named director of student health on the Danforth Campus in 1971. Four years later, the Medical Campus was added to her duties. In 2009, she was named Pioneer Woman of the Year by the Academic Women’s Network, a faculty organization dedicated to conquering barriers that face women in academic positions. She was an avid sailor and athlete and she designed and built a one-room cabin where her family spent many weekends. Each of her five children graduated from Washington University, and several grandchildren are alumni or current students.

Llewellyn Sale Jr., MD 40
Sale, a prominent physician for more than 55 years, died Monday, May 5, 2014. He was 99. A native St. Louisan, Sale graduated from St. Louis Country Day School before attending Yale University and Washington University School of Medicine. He trained at Barnes Hospital (as a chief resident and in medical services) and at New York Hospital. He began private practice in 1946 and was on staff at Barnes and Jewish hospitals. From 1972-92, Sale served as associate director of medicine at Jewish Hospital and on several hospital committees. He retired in 1996 as clinical professor of medicine. Sale was director of the university’s Student Health Services on the Danforth Campus from 1954-72. He received the Fellows Award from Jewish Hospital in 1991, the Faculty Achievement Award from the Medical Center Alumni Association in 1995 and the Distinguished Service Award from Washington University Department of Medicine in 2002. In 2010, the alumni association established a scholarship in his honor at the School of Medicine. Sale served as president or head of many area groups, including Washington University Medical Center Alumni Association, Jewish Family and Children’s Services, and Health and Hospital Division of St. Louis Community Fund. He was a member of the American College of Physicians, the American Medical Association, Southern Medical Association, Missouri State Medical Association, St. Louis Internists Club, the St. Louis Club, the St. Louis Society of Internal Medicine and the St. Louis Metropolitan Medical Society.

W. Thomas Thach Jr., MD
William Thomas Thach Jr., MD, professor emeritus of neurobiology, died Tuesday, July 1, 2014. He was 77. Thach, a neuroscience researcher and clinical neurologist, was a renowned expert and pioneering researcher on the cerebellum, a part of the brain that coordinates muscle movement and maintains balance. He was recognized internationally for his scientific contributions. Thach, who also was a professor of neurology and physical therapy, joined the Department of Anatomy and Neurobiology in 1975. He was named medical director of the Irene Walter Johnson Rehabilitation Institute in 1991. The next year, he became director of the section on neurorehabilitation in the Department of Neurology. He retired in 2012 and was named professor emeritus. An Oklahoma native, Thach earned an undergraduate degree from Princeton University in 1959 and then became a Fulbright fellow in physiology at the University of Melbourne in Australia. He received a medical degree from Harvard University School of Medicine in 1964 and completed his internship and residency at Massachusetts General Hospital. From 1966–69, he worked as a staff associate in the Laboratory of Clinical Science at the National Institute of Mental Health of the National Institutes of Health (NIH). He then returned to Massachusetts General Hospital, where he completed a clinical and research fellowship in neurology in 1971. He served on the Yale University School of Medicine faculty from 1971-75 before coming to Washington University. His life also was rich while not on campus. He loved hiking, camping, canoeing, hunting, reading literature and poetry, and playing music with family, friends and postdocs in his band, Taum Sauk.

If you would like to make a tribute in honor of any of the aforementioned alumni or faculty, please contact:
Pamela Buell, Washington University Medical Alumni and Development, Campus Box 1247, 7425 Forsyth Blvd., St. Louis, MO 63105, (314) 935-9691.
Thank you to the many alumni and friends who have supported Leading Together: The Campaign for Washington University through an estate gift, life income plan or other planned gift.

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Advocates for science

Junior faculty, fellows and students showcased their projects during the ninth annual Research Training Symposium and Poster Session this past fall in the Farrell Learning and Teaching Center. Here, participants gain experience communicating their research to a larger audience and receive critical feedback from mentors, colleagues and peers. Clockwise from upper left: medical students Miriam Ben Abdallah, Jordan Cole, Angela Lin and Stephen Fuest.
Mind & body  Sigrid Barklund, a fourth-year medical student and clinical mentor to first-year students, has practiced yoga for about seven years. Yoga, she said, keeps her “centered” as she juggles a rigorous academic and clinical schedule. Barklund demonstrated the range of her yoga poses last fall amid the greenery in Hope Plaza.