UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | FALL 2011

PITTMED



FACULTY OF WESTERN PENN'A MEDICAL COLLEGE, 1886

125 YEARS OF REMOVING AND PREVENTING THE ILLS TO WHICH FLESH IS HEIR

UNCERTAINTY IS NOT AN OPTION

Regarding the article "Uncertainty is Not an Option" in the last *Pitt Med*: In order to accurately diagnose ear infections in children, a pediatrician needs to master the use of the operating microscope. It took me about four to six months to learn this technique. There are several advantages: 1) removal of wax in infants and children; 2) visualization of the eardrum in infants and children; 3) ability to distinguish between acute otitis media and secretory otitis media; 4) removal of foreign bodies from ear and nose; and 5) suture removal.

Peter A. Statti
(A&S '59, MD '63)
Santa Maria, Calif.

I read Chuck Staresinic's article "Uncertainty is Not an Option." I only wish the doctors that my 2-year-old sees were aware of this. My son began getting low-grade ear infections last December. After three rounds of different antibiotics (and a bad reaction to one), we brought him back to the doctor's office on a Saturday morning. By then, we were seeing a third doctor at the same office.

Herein lies the story. Previous to the Saturday morning visit, we had visited two different doctors and been told that ear tube surgery and Rocephin shots were options. On that Saturday, we were told that my son would simply grow out of the infections. Three different doctors in the same office were recommending three different courses of treatment.

My wife and I had a 25-minute conversation with the third doctor about how confused we were. Still, we left wondering, *If we could not trust the doctors at the office for something minor (assuming the infection would clear up on its own), how could we trust the doctors if something more serious was wrong with our kids?*

Fortunately our son was re-checked later, and the infection had cleared up.

I hope that you can get your article to more doctors so that other parents are not put through the same frustrations that we were.

David Norvell
Charlotte, N.C.

STAY IN TOUCH!

We look forward to alumni news missives. And we gladly receive letters from our readers (which we may edit for length, style, and clarity). Drop us a line.

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CORRECTIONS

We regret that in an article about Howard Heit (MD '71) ("Howard Heit Speaks to an Epidemic of Undertreatment," Summer 2011), we reported his late wife's name incorrectly. She was Judith A. Heit (A&S '69). A corrected version appears on our Web site.



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PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE, FALL 2011 (SPECIAL ISSUE!)
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Maud Menten (c. 1923), one of the first scientists of international renown to join the faculty.

COVER STORY

125 Years of Removing and Preventing the Ills to Which Flesh Is Heir

11

"Although the propriety of establishing a medical school here has been sharply questioned by some, we will not attempt to argue the question. Results will determine whether or not the promoters of this enterprise were mistaken in their judgment and action. The city, we think, offers ample opportunity for all that is desirable in a first-class medical school, and if you will permit me to say it, the trustees and faculty propose to make this a first-class school."

—John Milton Duff, MD
Professor of Obstetrics, Western Pennsylvania Medical College, September 1886

COVER STORY BY BARBARA I. PAULL, ERICA LLOYD, EDWIN KIESTER JR., JOE MIKSCH, ELAINE VITONE, CHUCK STARESINIC, AND SHARON TREGASKIS

CONTRIBUTORS

In college, MIRIAM MEISLIK'S interests were all over the place. She took courses in art history, literature, information science, film, and audio production—"all these little things that made everyone say, *How are you going to make a living?"* she recalls. Little did Meislik know all those "little things" would align perfectly in the now-very-big field of media preservation and digitization. As archivist and photograph curator, Meislik manages media collections for Pitt's Archives Service Center. She frequently works with artists, researchers, television documentarians, and reporters—including the *Pitt Med* team ["125 Years of Removing and Preventing the Ills to Which Flesh Is Heir," p. 11]—in the hunt for just the right historical imaging. "I love my job," she says. "I can't imagine doing anything else."

BARBARA I. PAULL ["125 Years of Removing and Preventing the Ills to Which Flesh Is Heir"] wrote the book on Pitt med. Seriously. The author of *A Century of Excellence: The History of the University of Pittsburgh School of Medicine* (1986), Paull had been editor of the *University Times*, leaving the job in 1975 to "make my way as a freelance writer." That's when she submitted a proposal to write the story of the School of Medicine, and the rest is history. This magazine was happy to have her make a cameo for the school's 125th anniversary. Paull has also contributed to *Business Week* magazine and Quaker State Corporation as principal writer for its quarterly.

COVER

The medical college's first faculty members sport their 'staches, c. 1886. Pittsburgh photographer Paul Fallert took separate portraits of each of the professors, then artfully arranged and developed them together on one sheet. At the time, composite photography was in its heyday—it sure beat telling 22 people to sit still for several minutes. (Courtesy University Archives.) To put a face to the future of medicine, see our back cover.

PITTMED

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I always wanted to be somebody, but now I realize I should have been more specific. —Lily Tomlin



JOSHUA FRANZOS

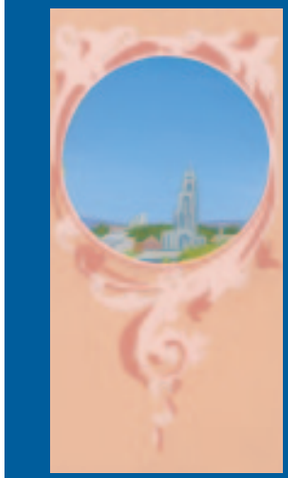
We can expect that in the next few years it will be possible to map your genome (all of the genes in your cells) for $1,000 or less, thanks to next-generation rapid DNA sequencing technology. Abnormalities in the genome would be seen, as well. With older technology, it would have cost on the order of a million dollars. As you can imagine, there's quite a buzz about this technology, which offers the possibility of identifying the risk of any given disease in an individual, as well as tailoring treatment of diseases to individual patients. But how much will it contribute to making you healthier—to the "personalized medicine" that we hear so much about? Is the technology really going to tell us with precision that any given mutation or polymorphism (the "genotype") means a given disease or disorder (the "phenotype") with certainty? Do our genes always hold our fate?

A report last year in *Science* by Robin Dowell (while at MIT) and others addresses the genotype-to-phenotype problem and is instructive: They saw that two nearly identical genomes managed to bring about two dramatically different phenotypes. The authors used two strains of budding yeast to assess the mechanisms leading to two different results for the same mutation. It became apparent that while the two genomes were indeed nearly identical, the two yeast strains had two different genetic "backgrounds." In this case, background refers to either rare polymorphisms (differences in expression of the same gene), complex combinations of genetic variation, or heritable effects like biochemical modifications (e.g., methylation) to DNA that don't involve actual changes to the molecular-building blocks (nucleotides) in the DNA. Dowell and her colleagues found that a complex set of background-specific modifiers influenced the mutation greatly.

This yeast model likely is very relevant to human disease, given that our most critical genes—those required for viability—are highly conserved in evolution, and they are present in yeast. ("Nature never throws away anything useful.") Moreover, the two yeast genomes are about as similar to each other as the genomes of any two humans.

How much biologically relevant information about us is encoded in our genomes? The genotype-to-phenotype question is a hot issue at the moment as we seek genetic patterns in the malignant cells of individual cancer patients that might tell us which specific drugs would kill the cells and which would not. This strategy, if successful, would revolutionize cancer treatment (and the prevention, diagnosis, and treatment of many other diseases). However, the yeast example tells us that new, rapid-genome-sequencing methods, even when coupled with profiling of the expression of our genes, will not be the end of the story. It is certainly true that in certain cancers, single genes can be mutated and that this has led to targeted drugs that block the effect of the mutation and extend life. Nonetheless, my intuition is that in most cancer, and most disease generally, the transformation of medicine will be far more challenging. After all, we and our cells have been evolving for billions of years. We are magnificent but almost unimaginably complex molecular symphonies of structure and function, and cannot be described as a collection of disconnected facts. These challenges needn't frustrate us. Instead, they should further drive us to imagine and experiment, using the power of science not only to ultimately transform medicine but, on the way, to offer context and meaning to our lives.

Arthur S. Levine, MD
Senior Vice Chancellor for the Health Sciences
Dean, School of Medicine



Devoted to noteworthy happenings

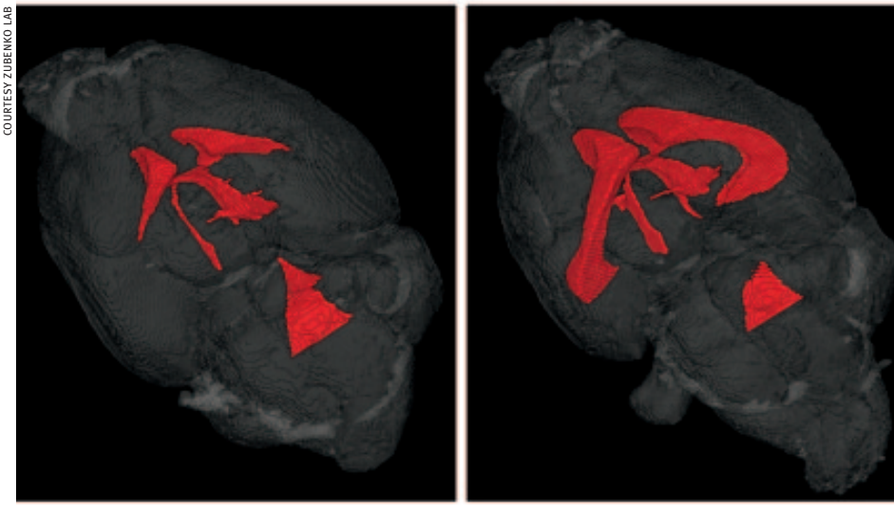
at the medical school

Mouse Models Depression

Major depressive disorder (MDD) causes personal suffering, affects families, and can lead to disability or even death, sometimes in the form of suicide. Pitt researcher and alumnus George Zubenko (MD '81 with a PhD from Carnegie Mellon University) is a professor of psychiatry in the School of Medicine. He has led a team that developed a genetically altered mouse that will enable deeper study of the affliction.

Zubenko's mouse model is based on the understanding that the familial form of MDD is linked to a mutation of a gene called CREB1. Zubenko replicated the mutation in an equivalent mouse gene. In addition to furthering the study of the brain mechanisms that lead to MDD, Zubenko says the methodologic approach used in developing the mouse model may be useful in the creation of models for other human diseases. ***—Joe Miksch***

COURTESY ZUBENKO LAB



Compared to the healthy mouse (left), Zubenko's mouse model (right) shows larger cavities, indicated in red—a sign of reduced brain tissue.

FOOTNOTE

Marvel-ous! Technology developed by Pitt's Jörg Gerlach, an MD/PhD at the McGowan Institute for Regenerative Medicine, appeared in Marvel Comics' *Avengers Academy* in May.

McGowan's Facebook page reports that "after two characters are badly injured in a building explosion, Hank Pym, who is one of the top scientific minds of the Marvel Universe, decides to treat their burns with the University of Pittsburgh's stem cell process"—Gerlach's skin cell gun.

STATE OF SCHOOL STRONG, YET THREATS LOOM

In May, Arthur S. Levine, senior vice chancellor for the health sciences and dean of the University of Pittsburgh School of Medicine, delivered his annual State of the School Address.

The school's 602 MD students, 308 PhD students, and 2,115 full-time faculty members, Levine says, are doing superlative work. The University faculty, driven by the med school, ranked fifth in the number of National Institutes of Health (NIH) awards granted between 2007 and 2010. Most Pitt MD graduates match with one of their top residency program choices (nearly 70 percent at top-tier programs). Faculty and student publication of research is at an all-time high. And, as the school develops partnerships abroad—the newest being with China's academic jewel, Tsinghua University—and with industry, its worldwide footprint is getting larger.

Levine says the school's greatest challenges come on the funding front, with NIH funding stagnant while state funds are cut. A video presentation of the address can be found at www.medschool.pitt.edu/about/index.aspx *—JM*



CAMI MESA

A&Q

Joel Greenberger Considers Fukushima Daiichi

Joel Greenberger, an MD, professor and chair of Pitt's Department of Radiation Oncology in the University of Pittsburgh School of Medicine, is also the director of the Center for Medical Countermeasures Against Radiation. He has appeared in these pages before. He and his team have developed a drug that, when administered to mice after exposure to radiation, significantly reduced radiation-induced death and adverse effects. In light of the Fukushima Daiichi reactor crisis in Japan, we thought it was time to talk with Greenberger again.

Long-term consequences in Japan?

Based on what we know … the easiest answer would be to say that long-term impacts are unknown. Unlike the Chernobyl disaster in 1986 and unlike other nuclear accidents, a huge confounding variable is the tsunami and flood damage. So you have two different categories of impact on the population in both the short term and long term. And so, we have to wait for more data.

On the handling of the crisis

I have nothing but praise for what the Japanese have done. The way that they handled this every step of the way was absolutely masterful, and I think it should be a lesson to us as to how a disaster like this should be handled.

On the safety of nuclear power

Our ability to detect radiation is getting much, much better. This makes people reluctant to push for more nuclear power plants. My own personal view is that we don't have enough. We should have twice as many nuclear power plants in this country. It's safe, it's clean, and it makes sense.

His questions for us

How concerned are you about levels of radiation exposure for you and your family? What would your level of concern be if you were asked to live near a nuclear power station? On that, I think you're going to get the reverse answer. There's a disconnect here … Some people are terrified of any radiation exposure, even when deemed "safe" by radiation safety officers, but are also willing to accept what their physicians tell them is a safe level. ***—Interview by Alexis Wnuk***

Faculty Snapshots

Brad Dicianno (MD '01, Res '05) recently won the AAP Young Academician Award from the Association of Academic Physiatrists. Dicianno is an MD and assistant professor in the Department of Physical Medicine and Rehabilitation.

The AAP praised Dicianno for his teaching, mentoring, his work as medical director of Pitt's Center for Assistive Technology and director of Pitt's Adult Spina Bifida Clinic, as well as his many publications in peer-reviewed journals.



Dicianno

Dicianno says he's grateful for the support of his chair, Mike Boninger, and mentor Rory Cooper. The academic environment they, and others, engender, Dicianno says, "is one of the many reasons I've never left Pitt since undergrad."

The School of Medicine's recently announced joint venture with Tsinghua University isn't its only foray into China. Pitt's Department of Pathology, through UPMC, has agreed to provide Web-based telepathology services for KingMed Diagnostics, China's largest independent medical diagnostic laboratory.

Department chair George Michalopoulos, an MD/PhD, says KingMed approached Pitt and UPMC about a year ago, seeking remote, second-opinion pathology consultations. The agreement, which spans three years, started late this summer. Michalopoulos says he expects that Pitt pathologists will consult on about 2,000 cases per month. Pitt's department is the largest of its kind, with 175 faculty members.



Handen

With a grant of $460,000 from Autism Speaks, Pitt will continue as one of 17 sites in the Autism Treatment Network (ATN). Benjamin Handen, a PhD associate professor of psychiatry and pediatrics at Pitt, is the principal investigator of the local site, which is a collaboration between the Center for Autism and Developmental Disorders at UPMC, Children's Hospital of Pittsburgh of UPMC, and the University of Pittsburgh Center for Excellence in Autism Research.

More than 230 families are enrolled in the local program, which supports diagnosis and medical evaluation for children and adolescents with autism spectrum disorder. ***—JM***

Treating Underserved Kids

Children's Hospital of Pittsburgh of UPMC has received $1.9 million from the U.S. Health Resources and Services Administration to expand its residency program for the primary care of underserved patients in both rural and urban areas. The five-year grant will cover the costs of training two residents per year. The program—Pediatric Advocacy, Leadership, and Service, or PALS—started in July with two residents. "A lot of the programming will be focusing on the kind of skills and attitude you need to provide effective primary care to the underserved," says Dena Hofkosh (Res '82, Fel '84), an MD and director of the Pediatric Residency Program.

—Megan Kopke



CATHERINE LAZURE

Neurons Don't Mature Fast

New neurons take about three or four weeks to develop in mice. It was assumed that the same timeframe applied to humans. But work by Judy Cameron—PhD professor of psychiatry at the University of Pittsburgh School of Medicine—and colleagues show that the process is much slower in primates.

Cameron, whose results were recently published in *Proceedings of the National Academy of Sciences*, shows that it takes up to six months for monkey granule cells (infant neurons) to reach maturity.

These findings, Cameron suggests, call into question the belief that it takes antidepressant medications three to five weeks to become effective, because that's how long it was thought to take for new neurons to generate in the presence of the drug.

Also, she adds, the more leisurely pace of neuronal development in primates allows a larger window for environmental factors to impact fetal development.

For example: "How does food the mother ingests change the development of brain circuits that control metabolism and body weight? There could be a lifelong effect on how you metabolize food and how likely you are to be chubby or thin," she says. *—JM*

VENTER GETS DICKSON PRIZE

J. Craig Venter is the recipient of the 2011 Dickson Prize in Medicine from the University of Pittsburgh School of Medicine, which will be awarded on Oct. 6 during the University's annual celebration of science and research—Science2011. Venter will also deliver the Dickson lecture at the festival's opening plenary session.

Venter, a PhD biologist best known for developing groundbreaking genomic discovery tools and sequencing the human genome, announced in 2010 that he and his team had constructed the first synthetic bacterial cell. He is founder and president of the J. Craig Venter Institute and founder and CEO of Synthetic Genomics. His lab focuses on creating synthetic biological organisms, developing applications related to this work, and unearthing the genetic diversity of the world's oceans. Venter received the 2008 National Medal of Science and is a member of the National Academy of Sciences. He is the author of *A Life Decoded: My Genome: My Life*. *—Chuck Staresinic*



VANCLIBURN FOUNDATION

PROF RECOGNIZED AS TOP PIANIST

Like his father before him, Barry Coutinho traded in a life in music for a career in medicine. In May, he placed third in the Van Cliburn International Piano Competition for Outstanding Amateurs. His performance of Maurice Ravel's *Gaspard de la Nuit* on a brand new Steinway Model D grand piano was an unanticipated success for Coutinho: "I played better than I expected. It seemed like I could do anything on that piano." Choosing a piece known as one of the most difficult of the early 20th century was an easy decision for the physician whose teacher in London's Guildhall School of Music & Drama studied under one of Ravel's own pupils. "I've played it so many times now that I knew it inside out," he says.

As a clinical assistant professor of family medicine in the School of Medicine and former chief resident of family medicine at UPMC Shadyside (Res '95), Coutinho has not performed often in the past decade. The Van Cliburn competition, which attracts the top amateurs from around the world, was one of his biggest performances in years: "I was worried about my competition experience but was very happy with the results in the end." *—Marc Melada*

Working on Caring

Holmes Morton, an MD, was the commencement speaker for the Class of 2011. He is cofounder with his wife, Caroline Morton, and executive director of the Clinic for Special Children in Strasburg, Pa., which specializes in the diagnosis and treatment of disorders of Amish and Mennonite children.

In his address, Morton touched on words spoken at a commencement long ago to illuminate his thoughts on what makes a good doctor:

"Learn to Care," in the sense of Dr. Francis Peabody's famous talk to Harvard medical students in 1926, titled, "The Care of the Patient." [Dr. Peabody said,] "One of the essential qualities of the Clinician is interest in humanity, for the secret of caring for the patient is in caring for the patient."

I understand that I am not by nature a friendly or caring person. I found that caring for a patient requires effort, thought. If I make learning about the life of the person being cared for [in the clinic] part of my daily work, the work of medicine becomes a rich human experience. Learning to care for the patient [as Peabody suggests] helps me value those I care for and adds to my sense that my work is meaningful.

Morton is a recipient of many medical honors, including the Albert Schweitzer Prize for Humanitarianism. Many of the clinic's patients suffering from a genetic condition called maple syrup urine disease were cured by liver transplants performed in Pittsburgh. *—JM*

FOOTNOTE

A science fair winner who is out of this world: **Andrew Abboud**, who will attend Pitt in the fall—with the promise of admission to the School of Medicine upon completion of his bachelor's degree—took "first award" in the recent Intel International Science and Engineering Fair. Abboud, of Ohio, won $3,000 for his research on "The Protective Effects of the Violacein Pigment against UV-C Irradiation in *Chromobacterium violaceum*." In honor of his achievement, Abboud will have a minor planet named for him. Really.



WHEN MRSA CAME TO HER DOOR

Michelle Sunjoo Lee is a gentlewoman and a scholar. And a musician. And an athlete. The energetic 17-year-old, who will be a senior at North Allegheny High School this fall, won the Young Epidemiology Scholars Competition in Washington, D.C., for research she conducted at Pitt. She worked under the guidance of Bruce Lee (no relation), an MD and assistant professor of medicine and biomedical informatics in the School of Medicine and of epidemiology in the Graduate School of Public Health, to design a computer model that examined the cost-effectiveness of testing high school athletes for MRSA.

Michelle approached Dr. Lee a few years ago after she was shocked to learn that MRSA, a highly antibiotic-resistant infection typically confined to hospitals, was claiming the lives of high school athletes across the country. There was even a case of MRSA at Michelle's school, though, fortunately, it was not fatal. "It was interesting to know that MRSA was actually coming to my front door, to my own school, so that piqued my interest even more," she says. As a tennis player and a rower, Michelle wanted to understand how the infection could be prevented in young athletes like herself.

During the two-year project, Michelle was able to determine the prevalence rate of MRSA at which routine testing of skin infections is cost-effective. Her research earned her first place at the national competition.

"I think the best part was getting to meet these other high school students from all around the country who were really passionate about their topics," she says excitedly. Never mind the all-expense-paid trip or the $50,000 scholarship she scooped up.

In addition to her scientific achievements, Michelle is also an accomplished pianist; she's given six solo performances at Carnegie Hall in New York City, as well as one at the United Nations.

Although both of her parents—Joon and Grace Lee (Grace is shown here with Michelle)—are professors at Pitt med, she's not sure that med school is in her future.

"In terms of career, I want to pursue kind of a combination of medical research, medical engineering, and public health," she says confidently.

She's certainly off to a good start. *—Alexis Wnuk*

—Photograph by Martha Rial

Explorations and revelations taking place in the medical school



Celedón has been wrestling with this question for his entire career: Why does asthma affect so many Hispanics? In a study of families in Puerto Rico, he recently discovered some surprising possibilities.

TOUGH ON TOTS

PUERTO RICAN CHILDREN MORE LIKELY TO HAVE ASTHMA IF PARENTS ARE STRESSED

BY MELINDA WENNER MOYER

When Juan Celedón began his medical internship at Lincoln Hospital in the Bronx in 1989, one thing struck him more than anything else. "I was impressed with how much asthma there was," he recalls. In the Bronx, hospitalization rates for the respiratory disease are five times higher than the national average, and death rates from it are three times higher. Asthma predominantly affects Hispanics, both in the United States and abroad—in particular, Costa Ricans and Puerto Ricans, the latter of whom have the highest lifetime asthma prevalence in the world. So Celedón, who hails from Colombia, recognized a research opportunity. Now, as the Niels K. Jerne Professor in the Department of Pediatrics in the University of Pittsburgh School of Medicine, chief of service in the Division of Pediatric Pulmonology, Allergy, and Immunology at Children's Hospital of Pittsburgh of UPMC, and director of Children's Center for Environmental Health, he is teasing out the potential causes of asthma in Hispanic populations. Among possible risk factors, he recently discovered that Puerto Rican children whose mothers or fathers suffer from stress-related conditions like depression are at a greater risk of developing the disease.

Celedón knew that some Puerto Ricans experience high levels of stress because of poverty and exposure to violence. Given their high asthma burden, he wondered whether the two factors might be related. In a study he published in 2010 with researchers at Harvard University, Virginia Commonwealth University, and the Behavioral Sciences Research Institute in San Juan, Celedón interviewed the parents of 339 pairs of Puerto Rican twins. The researchers interviewed the parents to see whether they had experienced symptoms of post-traumatic stress disorder, depression, or antisocial behavior, and the team also inquired about their children's respiratory health. Celedón and his colleagues found that 1-year-olds had more asthma symptoms if their dads suffered from PTSD, depression, or antisocial behavior. After controlling for a number of potential intervening factors—such as whether or not their parents had asthma—he found that kids aged 1 and 3 were also more likely to be diagnosed with and hospitalized for asthma if their mothers were depressed, and they were more likely to use oral steroids if their fathers were depressed.

No one yet knows why and how, exactly, parental stress influences asthma severity.

"It's unclear what's happening," Celedón says. It could be that stressed-out parents don't monitor or treat their children's symptoms as well as healthy parents do, ultimately leading to complications. But Celedón wonders whether parental stress could also be affecting certain genes in the kids, switching them on or off through the addition of methyl groups in an epigenetic process—a change in gene expression resulting from environmental influences—known as DNA methylation. Earlier this year, Swiss researchers reported that male mice separated from their mothers early in life—an intervention that causes them stress—give birth to offspring with abnormal DNA methylation patterns. It's possible, Celedón says, that such epigenetic changes could contribute to children's respiratory problems, and he plans to conduct more research to find out.

Also, obesity has long been known to increase asthma risk, and Celedón is striving to understand why. Earlier this year, he and colleagues at Harvard and Washington University in St. Louis found that inhaled steroids do not ease asthma symptoms as effectively in overweight and obese children as they do in normal-weight kids. Obesity could affect asthma risk for many reasons, but work Celedón published in 2009 suggests that genetics might be a common link: He and colleagues identified, based on a genome-wide linkage analysis, the very first gene associated with both body mass index (BMI) and asthma. The gene, called PRKCA, codes for a protein called protein kinase C alpha, which earlier research by other investigators suggests affects airway inflammation, mucous production, and the smooth-muscle contraction that causes wheezing.

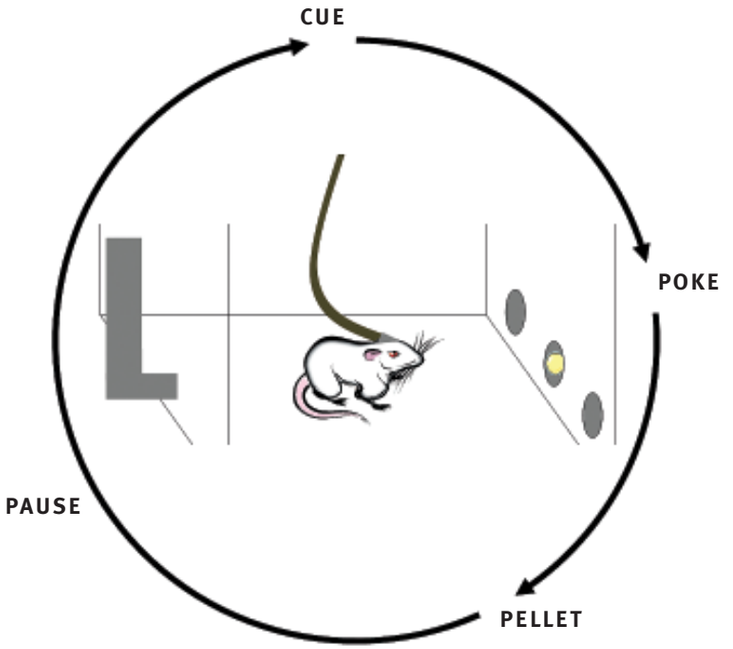
Although Celedón is focused primarily on understanding asthma's causes, "there is a lot of interest in trying to find predictors of asthma attacks, or who's at high risk," he explains. In a 2010 study published in *CHEST*, he and his colleagues developed a clinical score that predicts a child's risk of suffering an asthma attack based on answers to 17 yes/no questions about symptoms, medication use, and medical history. The team developed the score using data from a cohort of Costa Rican children and then tested how well it predicted symptoms in a group of American kids. "Much to our surprise, in spite of major differences in the type of health care and access to care between the two environments, we found that it performed relatively well," Celedón says. With this approach, "you don't need to obtain any lab data to try to assess who's at risk, so it could be used for primary care in developing countries"—and here, as well. ■

GETTY IMAGES

TINY BOPPER

TEENAGE THRILL-SEEKING AT THE CELLULAR LEVEL

BY KRISTEN COSBY



COURTESY MOGHADDAM LAB

Studying adolescence in the lab is like trying to hit a moving target, says David Sturman (PhD '11), a Medical Scientist Training Program student at the University of Pittsburgh School of Medicine. Although adolescence in humans lasts through most of the second decade of life, it spans from the fourth to the sixth week in rats. But in spite of these challenges, Sturman and his advisor—Bita Moghaddam, a PhD and University of Pittsburgh professor of neuroscience, psychiatry, and pharmaceutical science—have, for the first time, recorded and compared neuronal activity in awake adolescent and adult rats. Their study, which was published in the *Journal of Neuroscience* in January, provides new insight into the curious way adolescents weigh risks against rewards during this period of development. It also may offer insight into their vulnerability to developing disorders that could affect them throughout their lives.

The study of adolescent cognition and emotion is both challenging and rich with possibility. The symptoms of many psychiatric disorders—such as schizophrenia, anxiety, bipolar disorder, and drug addiction—often first appear during adolescence. Although these disorders cause great disruption to an individual's life and strain relationships with family and friends, the physical impact of these disorders on the brain is largely invisible. The brain's shift into a neurobiological disorder is subtle; the processes and interactions of the neurons change, while the number of neurons remains the same.

Previous studies have observed regional neuronal activity in adolescents using brain imaging, such as functional magnetic resonance imaging (fMRI) or electroencephalography (EEG). In contrast, Moghaddam and Sturman's study compares the activity of individual neurons in the orbitofrontal cortex—a part of the brain that calculates payoff and punishment when an individual is making decisions—in both adolescent and adult rat brains. They did this by surgically wiring electrodes into the rats, which had been trained to poke their noses through an illuminated hole for food, a basic reward-driven task. Logistically, Sturman says, all of the above was tricky, as was timing the surgery and recovery, in order to take advantage of the brief window of rodent teenhood.

Each rodent was placed into a box with three nose-poke holes. The team found that, overall, the brain activity in the adolescents was similar to that of the adults; but when the adolescents successfully stuck their snouts through the illuminated holes and received sugar pellets as a reward, the excitatory levels of their orbitofrontal-cortex neurons were two to four times higher than those of adult brains. The young rats' inhibitory levels, in contrast, were markedly reduced—a critical finding since neuronal inhibition is key to controlling the precise timing of neuronal activity.

These differences might help answer fundamental questions about adolescence: the thrill-seeking, the overreacting to upsetting or pleasurable experiences. Even when behavior may appear similar between the two groups, says Sturman, "the adolescent prefrontal cortex is in a different state than [that of an] adult."

Give an adolescent rat a treat, and you feed him for a day. Teach him to find it himself, and you can learn a lot about the neurobiology of teenage reward-seeking.

Inhibitory processes are essential for efficient communication between groups of neurons. The variable, frenzied neuronal activity detected in the young rats does not necessarily indicate that adolescents are more excited by rewards, says Sturman. Rather, there is something fundamentally different in how the neuronal networks compute, exchange, and store information regarding salient events. He and Moghaddam hypothesize that these processes are less efficient in adolescents than in adults, thus requiring more resources to process rewards—and their consequences. A better understanding of these differences in the exchange of informational currency might further illuminate normal teenage development as well as the various vulnerabilities that come with the territory, from addiction to mood disorders.

"This is really a magical period in which we can step in and prevent these diseases," says Moghaddam. Imbalances in the excitatory and inhibitory processes of neurons—which impair the exchange of information from neuron to neuron—have also been implicated in the onset of schizophrenia and other psychiatric disorders. Moghaddam says, "If we understand mechanistically what neurons, what receptors, what neuro-chemicals are involved, or are undergoing major changes during [adolescence], then we can understand what the trigger point is. And if we can understand that, then we are much better-equipped to control the disease and prevent the transition [into psychiatric disorders]." ■

UNIVERSITY OF PITTSBURGH ARCHIVES



125 YEARS OF REMOVING AND PREVENTING THE ILLS TO WHICH

FLESH IS HEIR

BY BARBARA I. PAULL, ERICA LLOYD, EDWIN KIESTER JR., JOE MIKSCH, ELAINE VITONE, CHUCK STARESINIC, AND SHARON TREGASKIS



"lthough the propriety of establishing a medical school here has been sharply questioned by some, we will not attempt to argue the question. Results will determine whether or not the promoters of the enterprise were mistaken in their judgment and action. The city, we think, offers ample opportunity for all that is desirable in a first-class medical school, and if you will permit me to say it, the trustees and faculty propose to make this a first-class school."

—John Milton Duff, MD
Professor of Obstetrics, September 1886

More than three decades after the city's first public hospital was established, after exhausting efforts toward a joint charter, Pittsburgh physicians founded an independent medical college, opening its doors in September 1886. This congested industrial city—whose public hospital then performed more amputations and saw more fatal typhoid-fever cases per capita than any other in the country—finally would have its own pipeline of new physicians for its rising tide of diseased and injured brakemen, domestics, laborers, machinists, miners, and steelworkers from around the world, as well as the families of its merchants, professionals, and industry giants.

Today more than ever, Pitt med people are coming up with ways to, as Professor Duff put it, prevent and remove "the ills to which flesh is heir." We've saved those stories for another day. On these pages, we offer some lesser-known moments in the early history of the city and school along a steady rise to prominence.

SHOWN HERE: **Members of the first faculty of the medical school, 1886.**



JOSEPH WARIN, ENGRAVED BY ANTOINE-FRANCOIS TARDIEU, 1826.

LEFT: *Plan of the Town of Pittsburg*, by cartographer Joseph Warin, 1796. PP. 13 & 14: A lithograph of the bustling new town in 1859.

THE LAND BETWEEN THE RIVERS



This land between the rivers was the frontier, requiring an arduous journey over the mountains or a risky river approach. The terrain was hilly with untamed streams rushing through steep ravines. Many were attracted by Pittsburgh's lush, wild landscape and its bountiful waterways. Settlers built on "The Point," facing the port on the Monongahela River. Centuries later, this settlement would become a capital of medicine. Some glimpses of its early health history:

At Fort Pitt, the British built two rough shelters in 1761 for a military hospital. After the war, a few physicians remained to serve the civilian populace.

The local population was diverse. Blacks helped build Fort Pitt; both freemen and slaves lived within the city. Delaware Indians had a village on the banks of the Allegheny River, near today's Lawrenceville. Iroquois and Shawnees also made their homes in the area, though these peoples were decimated by European diseases such as smallpox, influenza, and malaria.

A public water system, built on the banks of the Allegheny River in 1820, was ineffectual. Refuse and heavy rains transmitted waterborne diseases directly to the public, and the water itself was unfiltered. Repeated epidemics of smallpox, Asiatic cholera, and typhoid fever plagued the city.

Smallpox, the most feared plague, caused 74 deaths in 1828, despite quarantines. Asiatic cholera spread throughout the nation in 1832. To prepare, Pittsburgh built a temporary hospital and a dispensary, cleaned the streets, and removed garbage; still 105 died from cholera that year.

As Pittsburgh grew, the quality of the water supply worsened. Allegheny River pollution was visible to the naked eye. In 1907, 5,652 cases of typhoid fever were reported, 648 of them fatal. As the outcry for clean water grew, construction began in 1905 on a slow sand filtration plant in Aspinwall. The city began getting treated water in 1908, and the instances of typhoid fever diminished significantly in the next few years.

By 1840, Pittsburgh had become an industrial behemoth of iron and glass making, river travel, coal mining, and natural gas. Airborne coal dust, polluted rivers, and the smell of the slaughterhouse befouled the once-pristine environment.

In 1787, locals gave a nod to education with a preparatory school, the Pittsburgh Academy. It was reincorporated in 1819 as the Western University of Pennsylvania, which was later renamed the University of Pittsburgh.

A disastrous 1845 fire that began in a downtown shed demolished much of the city, including Western University of Pennsylvania. The school was rebuilt on Duquesne Way, but fire struck again in 1849.

Described in 1820 as "a pleasant and flourishing town," Pittsburgh later became known as an industrial den, dark with the effluvium of its industries. While many believed coal dust was actually healthful, keeping one free from malaria and lung ailments, the wealthy boarded trains each evening to their homes in the suburbs of East Liberty, Point Breeze, and Wilkinsburg. Those who lived nearest the mills, not surprisingly, were reported to have the worst health. By 1913, pneumonia was the city's primary cause of death. (Today, after two renaissances, Pittsburgh has repeatedly been



JAMES T. PALMATARY, *BIRD'S EYE VIEW OF PITTSBURGH, ALLEGHENY, BIRMINGHAM, SOUTH PITTSBURGH, SLIGO, MANCHESTER AND LAWRENCEVILLE*, 1859. TINTED LITHOGRAPH ON FOUR SHEETS. DUQUESNE CITY CLUB.

voted the nation's "most livable city." Its air quality has improved markedly, but the region still fares poorly in terms of particulate matter.)

In 1847, Pittsburgh—about 90 years old—still had no public hospital. Physicians held a public meeting to whip up support for a proposed institution, and the state legislature passed an act of incorporation in 1848. But the hospital's realization was still years away.

Mercy Hospital, now situated on The Bluff near Duquesne University, was the first hospital founded by an order of Catholic nuns called the Sisters of Mercy and the first permanent hospital in Pittsburgh. In January 1848, the sisters admitted a sick boatman to the hospital. He had typhus. They treated the man and admitted 18 other typhus victims. When the epidemic ended a few weeks later, 15 patients remained alive, but the entire nursing staff—four Sisters of Mercy—had died.

The city's first public hospital, Western Pennsylvania Hospital, completed in 1850, was built on a hilly, 24-acre tract overlooking the Allegheny River. It stood empty for two years; no funds were available to furnish and equip the building. Once it opened, patients were brought to West Penn up the steep hillside via 28th Street by a horse- or mule-driven ambulance crossing the Pennsylvania Railroad tracks at Liberty Avenue.

Industrial accidents, especially those suffered by railroad employees, accounted for many of the admissions to West Penn. Railroad workers were often injured by the hand-operated car brakes or from the link-and-pin system for coupling cars.

During the Civil War as many as 1,500 wounded Pennsylvania soldiers were treated in the main wards of West Penn or in tents on the lawns. For a decade after the war, West Penn primarily treated veterans.

Before Pittsburgh had a medical school, Western Pennsylvanians seeking a medical education had few options. They could travel to the East Coast for training. Some went to Scotland's Edinburgh University. Some apprenticed themselves to local physicians. Medicine was largely unregulated, so anyone could go into "business," and there were many forms of quackery.

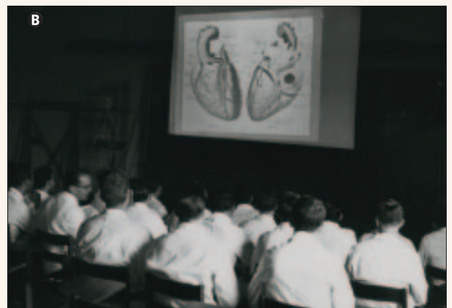
A group of physicians and surgeons, mostly practitioners at the Western Pennsylvania Hospital, sought harbor with another institution that would support a medical college. The group was repeatedly rebuffed. Western University refused to give up space for a dissection room or an anatomy room. When the physicians next sought a formal alliance with the University, the trustees said, "No."

The medical men did not give up. They decided to form a private college themselves. On June 4, 1883, Western Pennsylvania Medical College was chartered, and 250 shares of stock were issued at $100 each. The sale of stock functioned as an endowment.

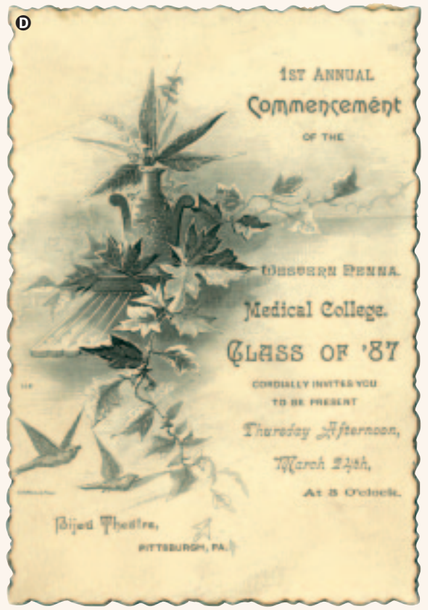
The Western Pennsylvania Medical College enrolled its first class in 1886. The founders bought land adjacent to West Penn Hospital, at 30th and Brereton Streets, in what is now Polish Hill. Although West Penn Hospital had refused to sponsor the Medical College, it offered the hospital wards as a clinical facility for students. ■











THIS PAGE: UNIVERSITY OF PITTSBURGH ARCHIVES

ABOVE: Surgical operating theater at Mercy Hospital, c. 1910.
A Anatomy Department staff, 1953.
B Students attend a lecture in Pennsylvania Hall. Date unknown.
C Joyce Barraclough, member of the Virus Research Laboratory staff, opens an inoculation egg to remove the fluid containing influenza virus. Date unknown.
D Graduation announcement, 1887.



E–H, J, L: UNIVERSITY OF PITTSBURGH ARCHIVES

E

THE EARLY YEARS

The medical college was housed in a new five-story building, completed in 1885, on property abutting West Penn Hospital. (An underground passageway linked the two buildings.) Most impressive was a well-lighted, two-story post-mortem examination room. Other features were a lecture room, a dissecting room, several laboratories, and a museum. The museum, a gift from Albert G. Walter, an orthopaedic surgeon, held several hundred bones "illustrative of deformities," plus tools and instruments invented by Walter.

Applicants to the new college needed only a diploma from a high school or a normal school.

Fifty-seven students enrolled in the college's first class. A hundred dollars per year gave students access to all lectures and clinics. Other annual fees: matriculation, $5; practical anatomy, $10. The graduation fee was $25.

Students attended 14 clinical lectures each week and observed hospital surgery. Much of the work was hands-on from the beginning.

In the college dispensary, the hospital wards, or the City Alms House, students saw a panoply of medical ills: venereal diseases, mental and nervous complaints, childhood illnesses, eye and ear irregularities, conditions requiring surgery, and nose, throat, and skin disorders.

Records are conflicting about whether the school first offered a one- or two-year degree; but the school soon expanded to a three-year program, with a fourth year recommended.

Most of the professors at the college—not just after its founding but in later years, too—were unpaid volunteers. They were prominent practicing physicians.

In 1892, the medical college once again went looking for an affiliation with Western University of Pennsylvania. This time, Western was interested. After all, the 250 shares of medical college stock had grown to 1,000 shares. The "terms of union" were attractive. The medical college would be self-governing and self-sustaining, at first anyway. Western University gained partial nonvoting ownership of the medical college that year, with the option to take total ownership in the future.

In 1908, Western University of Pennsylvania was formally renamed the University of Pittsburgh under Chancellor Samuel Black McCormick. The University purchased 43 acres of hillside land in Oakland, known as Schenley









COURTESY ROBERT CHASE



Farms, for its new campus. That same year, the Western Pennsylvania Medical College became the property of the University of Pittsburgh.

The School of Medicine moved from Polish Hill to Pennsylvania Hall, located on the new University of Pittsburgh campus, in 1911.

As third dean of the medical school, Thomas Shaw Arbuthnot (appointed in April 1909) was an inspired choice. He was somewhat in the mold of Teddy Roosevelt. Arbuthnot came from a wealthy family, was a man of ideas and action, and was even a big game hunter. During his 10-year tenure, he transformed the medical school by modernizing the curriculum, building a top-notch faculty, and giving a sense of direction for the future.

At a time when only 15 medical schools required applicants to have anything beyond a high school education, Arbuthnot quickly raised entrance requirements to a minimum of two years of college and transformed the faculty by hiring young, promising medical scientists. (His instincts were excellent: Physiologist/pharmacologist C.C. Guthrie, for example, transformed blood vessel surgery. Oskar Klotz, chair of pathology, published extensively and recruited excellent faculty.)

The famed Flexner Report of 1910, which found that a large number of med schools had created an "enormous overproduction of undereducated and ill-trained medical practitioners," suggested that the 155 colleges of medicine in the United States should be cut to 31 medical departments within large, well-run urban universities. Flexner was astonished by how well Pitt's School of Medicine fared under Dean Arbuthnot. *Since the present management took hold last fall, the admission of students has been much more carefully supervised, the building has been put in excellent condition, laboratories for chemistry, physiology, bacteriology, and pathology have been remodeled and equipped with modern apparatus … . The entire atmosphere of the institution has clarified: students may be found actually studying in the room in which under other conditions last year "four dozen wooden chairs were broken up" in boisterous horseplay.*

In 1913, the School of Medicine received an A+ rating from the American Medical Association's Council of Medical Education, putting it in league with medical colleges at Johns Hopkins, Harvard, and Yale.

COURTESY GENE STARZENSKI





Ⓔ Original home of the Western Pennsylvania Medical College on a hillside at 30th and Brereton streets in Polish Hill. In later years, as the school gained traction: Ⓕ Groundbreaking for Scaife Hall with Alan Magee Scaife and Sarah Mellon Scaife holding the shovel, 1954. Ⓖ Frank Dixon (middle) and colleagues, c. 1950s. Ⓗ Children's Hospital of Pittsburgh. Date unknown. Ⓘ Milt Dupertuis (center), inaugural head of Pitt's plastic surgery program, and residents examine a patient with a cleft lip repair in 1958. Pitt's program quickly became a coveted training ground. Ⓙ Aerial view of the Oakland campus, c. mid-1940s. Ⓚ Peter Safar (second row, far left) with the staff of Freedom House Enterprises Ambulance Service at their Hill District headquarters in 1975. Ⓛ Jack Meyers in action. Date unknown.



During the flu pandemic of 1918–1919, Pitt students were conscripted into the Student Army Training Corps for the war in Europe, and many fell sick soon after.

WARTIME AND OTHER CHALLENGES OF A CENTURY

In 1917, when the United States entered World War I, Dean Thomas Shaw Arbuthnot, by then a major in the army, took a leave of absence from the medical school to spend 15 months on French soil, along with other members of the teaching faculty. Base Hospital 27, organized and staffed by the University of Pittsburgh School of Medicine, was sent to Angers, France, in September of that year. The group was housed in Mongazon seminary. The hospital was intended to hold 500, but during one week, 2,300 casualties arrived. The influenza pandemic felled as many as the enemy did.

Acting Dean Ogden Edwards Jr. led the school through the challenges of 1917 to 1919, including a regional onslaught of influenza. More than 23,000 Pittsburghers came down with the flu, and third- and fourth-year medical students were conscripted to care for those in hospital emergency wards.

Edwards, the acting dean, had an active interest in public health. As a former director of the City's Department of Public Works, he had pushed for milk-production standards. He suggested that the faculty use its skills to address safety problems in the mills and coal mines. Edwards, like Dean Arbuthnot before him, thought working with the community on such problems was important even though, according to medical education historian Martin Kaufman, it was "generally assumed by members of the medical profession that doctors who devoted their time to the treatment of industrial workers … were not qualified to pass judgment on medical problems."

Wartime students faced stiff academic discipline, and dropouts were automatically drafted. When student Philip Hench (who later won a Nobel for his work on cortisone) fell asleep in class, he was threatened with expulsion but got off with a sharp rebuke.

In a 1918 memo, Acting Dean Edwards described his vision of a medical center, suggesting that "a medical school building, a laboratory of hygiene and public health, a research laboratory, ... a small general hospital, an eye and ear hospital, a children's hospital, a general dispensary, a psychopathic hospital" should be located together on the H.K. Porter property (a 12-acre site a little further down the hill from the existing Pitt campus). If a general hospital were built there, it would be in close proximity to the medical school. Dean Edwards boldly contacted Mr. Porter, asking him to name his price. Mr. Porter was not amenable to the proposal for some time. The University eventually bought the Porter site for $182,500 in October 1921.

On his return from the war, Arbuthnot tendered his resignation and could not be convinced to stay on as dean. When Raleigh Russell Huggins assumed the deanship, the creation of a medical center became his top priority. He wanted "first-rate practitioners and researchers" a stone's throw from the classrooms. He was encouraged by Chancellor John Bowman, who had made important friendships with Andrew and Richard B. Mellon; they all would share the dream for the medical center and University.

The medical center proceeded by fits and starts, especially during the Depression. Magee Hospital, in its original location (a former mansion), was the first to affiliate with the University. On the Porter property, Children's Hospital opened in 1926, followed by the Eye and Ear Hospital in 1934. Falk Clinic, an outpatient facility funded by brothers Maurice and Leon Falk, was dedicated in 1931.

Presbyterian Hospital, the much-needed general facility, was the toughest case. Presbyterian administrator Hugh Thompson Kerr, an MD, recalled spending an evening with Dean Huggins, who urged him to make Presbyterian Hospital part of the medical center: "[Huggins] kept saying, 'The idea is right, and it is bound to be realized.'" But because of a lack of money, it took 15 years to complete the hospital building, which opened finally in 1938. The east wing of that structure was built and occupied by Women's Hospital and completed in 1939.

One other hospital, Western Psychiatric Institute and Clinic, was made possible by an act of the Pennsylvania General Assembly in 1931. It was located on University property, at Desoto and O'Hara streets. Its primary purpose was to treat those who could improve after about four months in residence.

In 1943, the military took over floors 2 to 14 of Pitt's Cathedral of Learning, and air-crew trainees moved in. A couple of medical students were hired to work with Henry "Doc" Carlson, Pitt's physician for students (as well as varsity basketball coach), to treat the trainees. Eventually, the military inducted all the med students as privates first class. By then, 6,000 University faculty, staff, and students were serving at home and abroad.

By the time Huggins had assumed his deanly responsibilities in 1920, the 13-year-old Pennsylvania Hall was already cramped and inadequate. (Among other issues, the skylight leaked rain on students in the dissecting room.) After William S. McEllroy, the school's fifth dean, was appointed in 1938, the school expanded to the old Mellon Institute. But it was not until June 29, 1954, that Mrs. Alan Magee Scaife (Sarah Mellon Scaife) turned the first spade of earth for the 10-story, $15 million School of Medicine building that four years later would bear her husband's name.

Dean McEllroy put his energies into bringing funded research to the school. (His secretary, Edith Glenn, managed day-to-day activities and knew all the students.) A Pitt medical school graduate himself, McEllroy (MD '16) wanted national recognition for the school.

McEllroy's determination to hire promising researchers bore fruit in the postwar period. His first full-time clinical appointee, Thaddeus Danowski, was an endocrinologist specializing in childhood diabetes. A $500,000 grant helped him move his group to Children's Hospital in 1947.

Two years later, Dean McEllroy cobbled together money from four different departments in order to hire Jonas Salk, a young virologist working on the influenza virus. Salk's lab was in the basement of Municipal Hospital (which, at the time, was not even a part of the Pitt campus). Salk maneuvered directly for what he wanted—more laboratory space, more independence, more money for research. He recruited virologist Julius Youngner and other key team members. Skirting University protocol, Salk negotiated directly with Harry Weaver, research director of the National Foundation for Infantile Paralysis, to get grants. Weaver felt instinctively that Salk had the drive to seek a cure for polio, the disease feared by so many families.

Scientists on the polio-vaccine team inoculated themselves first, then their own children, before doing field tests. In 1952, children at what was then the D.T. Watson Home for Crippled Children, a rehabilitation center, received the vaccine. On April 2, 1955, scientists at the University of Michigan confirmed that the Pitt team had created a vaccine that was "safe, effective, and potent."

The polio-vaccine team's accomplishment set the tone for the school's future. In the decades after, the school would attract, among its faculty and student body, an array of clinical stars and astoundingly good physician-scientists who would change medical science forever. Beginning on p. 24, we share our Pitt-med-centric view of defining moments in medicine. ■





A, C, D: UNIVERSITY OF PITTSBURGH ARCHIVES. B: COURTESY STEWART SELL





Ⓐ Having completed their training, soldiers prepare to depart in front of Soldiers and Sailors Memorial Hall & Museum. June 11, 1918. Ⓑ In August 1945, U.S. marines and medical personnel receive Japanese B encephalitis vaccine at a field hospital in Okinawa, where Oliver M. Sell (MD '26) served as commander. The entire medical school served in either the army or navy, as well. Ⓒ Jonas Salk with lab technicians, c. 1954. Ⓓ Children receive polio inoculations, c. 1955.



Early Pitt medical coeds pose for a group shot in *The Owl*, 1910. Four classes, 1909–12, are represented, yet for three of those years the school barred additional women from enrolling.

OPPORTUNITY DIDN'T ALWAYS KNOCK

The medical college was coeducational until 1909, when it barred women from admission.

Amelia Dranga, a local physician who headed the Women's Medical Society in Pittsburgh, voiced her opinion about the ban on women to the Chancellor and others, including the *Pittsburgh Press*: *The argument advanced for refusing women's admittance is that it is embarrassing for the women and men to study medicine together. Bosh! If women and men can be embarrassed by studying medicine together, then their places certainly are not in the medical profession.*

In the face of declining enrollments (because of stricter entrance requirements), the University board capitulated, resolving in its June 1912 meeting that *It will be possible to receive young women students in this school, even though special facilities which it is hoped may be made later, are not yet possible.* Three women entered the freshman class in 1913. Today women make up about half of the student body.

In 1901, the School of Medicine graduated its first African American MD: Allen Gilbert Gantt, who practiced medicine in Pittsburgh for half a century. He was born in South Carolina and served as a pastor there for two years before he came to Pitt. At the time of his death in 1950, he was medical advisor at the Davis Home for Colored Children, an orphanage in Point Breeze. Gantt and fellow African American alums Harrison M. Brown (MD '04), Charles Henry Carroll (MD '06), and James Charles Gill Fowler (MD '06) were all founding members of Rho Boulé, the local chapter of Sigma Pi Phi. The fraternity is still going strong to this day, supporting social action and public-policy efforts in Pittsburgh.

The same opportunity didn't arise for a Black woman for several decades, until Harrisburg, Pa., native Elaine Morris (MD '75) graduated.

By 1915, about a half dozen African Americans had made the school's alumni roster. Then, inexplicably, Blacks were barred for some 30 years. This shift reflected the grim national picture in the Jim Crow era. As late as 1968, only 266 Blacks were enrolled in med schools across the country—all but a few dozen of them at historically Black universities.

Enrollment for Jewish students was a slow, uphill climb, as well. According to *To Good Health and Life: L'Chaim (A History of Montefiore Hospital of Pittsburgh, Pennsylvania, 1898-1990)*, "There was no question. For the Jew aspiring to a medical career," said Sidney Kaufman (MD '41), "it was a hostile environment. Medical schools limited Jewish admissions severely." He was one of five Jews to graduate in his class of 55 students.

In the wake of civil rights protests, American undergraduate and graduate schools made unprecedented efforts to diversify enrollment in the early 1970s. Pitt med alums from that time report they'd been offered numerous scholarships from other schools. But to their disappointment, during their interviews, most of those program administrators confessed they were accepting only one or two African American students at a time. Pitt outpaced them all, admitting 15 Black students in 1970.

Unfortunately, this promising jump in the numbers wasn't sustained—the '70s were roller-coaster years for enrollment of students from underrepresented groups. Black students—who, in addition to the rigors of their studies, were practically running the school's diversity recruitment effort themselves at that time—called for reinforcements. They finally got them in 1979 when a new position was created: assistant dean for minority affairs.

Enrollment among underrepresented groups shot up from 12 schoolwide in 1978 to 61 students by 1984, thanks to William Wallace and Carolyn Carter, the first two to fill the assistant dean role. Wallace discovered that some prospective students who were denied interviews at Pitt wound up attending other prestigious medical schools; this helped him make a case for changing the review process at Pitt.



MEDICAL ALUMNI ASSOCIATION



In the ’70s, Jackson Wright (MD ’76, PhD ’77) became the first African American to earn both an MD and PhD from the School of Medicine. Wright is now a professor of medicine at Case Western Reserve University. A seasoned clinical researcher focusing on agents that lower hypertension and cholesterol, he’s been a key player in nearly every major clinical-outcome trial conducted in African American populations in the past two decades.

Sandra Murray, professor of cell biology and physiology, became the School of Medicine’s first African American female tenured full professor in 1999. Murray has been a seminal contributor in the field of cell-to-cell communication. (When Murray first started haunting science fairs in grammar school, she was in it for the ticket out of class. Little did she know they’d turn her into a lifelong learner and a science lover.)

As a Pitt med student, Jeannette South-Paul (MD ’79) led a group that established the Black Bag Award, which honors a faculty member each year for work with Pitt meders from underrepresented populations. As Pitt’s Andrew W. Mathieson Professor and Chair of the Department of Family Medicine, she has herself won a number of awards for community service, research excellence, teaching, and mentoring, including the 2004 McCann Scholar Award from the Joy McCann Foundation. South-Paul was the first woman to serve as a permanent chair of a department in Pitt’s School of Medicine.

There’s been a bit of a Pittsburgh dynasty in SNMA (Student National Medical Association), the nation’s oldest and largest student organization focused on the needs and concerns of medical students of color. Several Pitt meders have served as national and regional SNMA officers in the past decade, including Leon McCrea (MD ’06), Aderonke Omotade (MD ’03), Nikkisha Prentice (MD ’06), and J. Nadine Gracia (MD ’02, Res ’05), who’s now chief medical officer for the U.S. Department of Health and Human Services’ Office of the Assistant Secretary for Health.

The school now hosts several efforts to spark interest in medicine among young people from underrepresented groups. Launched in 1974, Pitt’s Medical Explorers program—which teaches teens and tweens about the health professions—is the longest-running among the some 10,000 groups around the country. At 131 members last year, Pitt’s is probably also among the largest. At least eight explorers have gone on to don white coats in the School of Medicine, and dozens of others have in med schools elsewhere. ■





THE OWL, 1907

Ⓐ Jeannette South-Paul (top) with colleagues, May 25, 1979. Ⓑ Maud Menten (c. 1923) was among the first scientists of international renown to join Pitt’s faculty. (See p. 30.) Ⓒ Charles Henry Carroll (MD ’06) and Ⓓ James Charles Gill Fowler (MD ’06), two early African American graduates of the school, shown in their yearbook photos. Ⓔ Members of the Class of 1974 on graduation day (from left): William Hicks, Herbert Chissell, Brian Bowles, Everett Cantrell, Marion Williams, Charles Hefflin, John Houser, William David Moore, and William Cleveland.



COURTESY WILLIAM CLEVELAND

THE OWL, 1910-

UNIVERSITY OF PITTSBURGH ARCHIVES

EX HOC SEMINE NOSTRA GLORIA

(FROM THIS SEED OUR GLORY)

What follows are excerpts from the first lecture given to students of the Western Pennsylvania Medical College in September 1886. Chair of obstetrics, John Milton Duff, an MD, did the honors. Duff, who raised $15,000 to be put toward a hospital for the South Side, taught humility and respect for science and nature; he was also a product of his paternalistic times.



Duff

GENTLEMEN:

You enter a profession of which you may well feel proud. Great has been medicine's work in the past! What may we expect of it in the future! In your labor the delight of acquiring knowledge and intellectual power will be compensation. There will be a gratification in searching for the intricate beauties of God's most holy work, while satisfaction will abound everywhere in contemplating the gracious supply of means for removing and preventing the ills to which flesh is heir.

Entertaining in its study, often very difficult in its practice, we are sorry to say obstetrics does not always receive the consideration its importance demands. A large proportion of the laity deem the duties and responsibilities so slight that they regard any ignorant pretender ... as a person thoroughly competent to preside over the lying-in chamber. ... It is obligatory upon the practical obstetrician to acquaint himself intimately with every pathological change of physiological process which may or should take place from the moment of conception until the mother, after a return to a normal condition, walks forth from the lying-in chamber with the child of her womb pressed to her bosom. After delivery, dangers surround her on every hand. Not only the state of the solids and fluids demands attention, but the organic changes which must take place in every lying-in woman need the closest and most intelligent watchfulness.

In the study of obstetrics one of the subjects which demands your special attention is the peculiarities of sex. It is in domestic life that woman shows to greatest advantage. … In this home relation you will have the greatest opportunity to study her peculiarities. The family hearthstone is her throne, and there she wields the scepter of power. ...

What can be more inviting than to watch the development of the human ovum as it passes through its many transitions, from the time it is grasped by the fimbriated extremities of the Fallopian tube until—after months of an interesting developmental existence in the uterus—it at last through the powers of nature is expelled and comes forth to the world a perfectly formed human being breathing the breath of life.

Beautiful as is the uninterrupted display of nature under these circumstances, … it will be necessary for you who expect to become practitioners to interest yourselves in the abnormalities and pathological conditions which often occur. They should be of peculiar interest to you. There is an importance attached to them which calls for the most careful study; an importance which you will not and cannot appreciate until, perhaps far away from instructor and associates, you will be called upon to face with fear and trembling.

Picture to yourselves a scene: A happy household, joyfully anticipating the advent of a bright and tender baby to add new charms and new joys. … Suddenly the sunshine of their happiness is darkened. … Listen to the wail that goes up from those motherless children—while the ignorant pretender standing by is dumb to all entreaties, forced to inactivity by his incompetence … call upon the rocks and the mountains to fall upon him and hide him from the presence of his God!

Gentlemen, I would that I could let fall upon you words of fire to impress upon you the sacredness of the obligations you take upon yourselves when you announce to the world your readiness to practice medicine.

Do not allow yourselves to think a mere cursory knowledge of your subject is sufficient … nor that your own ingenuity will supply all deficiencies and add perfection to every excellence. Such a course will consign you most certainly, and soon, to well-merited oblivion, where you may ponder sadly over the melancholy memorial of time misspent or of industry exercised unavailingly. You will find nature a wonderful obstetrician. If let alone, many times she will surmount difficulties in a manner which would put the blush of shame on your best-directed efforts. ■

Editor's Note: While Professor Duff pontificated on the "peculiarities" of the female sex, women of Pittsburgh were coming together to build and support much-needed hospitals for the city (see opposite page), and then some.



The formidable Mary Copley Thaw (c. 1910)

COURTESY UPMC SHADYSIDE

WOMEN OF STEEL

THE "GENTLER SEX" TRANSFORMED HEALTH CARE IN PITTSBURGH

On Feb. 7, 1898, Annie Jacobs Davis called together 17 of her neighbors in Pittsburgh's lower Hill District. Like Davis, a 33-year-old mother of six born near Moscow, every woman in the room was a Jewish immigrant from Eastern Europe. And like Davis, they held the principle of charity—*tzedakah* in Hebrew—in high esteem.

At that meeting of like minds, the women formed the Hebrew Ladies Hospital Aid Society (HLHAS), with annual dues of $5. Their charter, signed the next year, vowed "to assist and provide the deserving sick, injured, and disabled with proper medical and surgical attention and hospital treatment," and when its funds would permit, open a hospital—a move that would also give Jewish physicians, who otherwise faced practice restrictions, a hospital to staff.

The HLHAS campaigned tirelessly and creatively. By 1903, they were providing care for 70 patients annually. Through picnics, carnivals, and myriad other events, they raised more than $25,000 to support the establishment of Montefiore Hospital, which opened in 1908.

Perhaps Davis knew of Louise Wotring Lyle, a 56-year-old MD who, in 1893, had founded Presbyterian Hospital in a three-story house on what's now Pittsburgh's North Side. Or perhaps she took note of the Ladies' Charitable Association of the Homeopathic Hospital—now UPMC Shadyside—formed in the 1860s.

In the latter half of the 19th century, as the city's population exploded, the middle- and upper-class women of Pittsburgh instigated an unprecedented boom in hospital formation and construction. The Irish Catholic Sisters of Mercy had, since 1847, operated the city's first civilian hospital. Two years later, four German Lutheran deaconesses immigrated to help start and work in the Pittsburgh Infirmary (now UPMC Passavant). In the 1880s, women formed the board of directors of Children's Hospital of Pittsburgh, a project conceived in 1883 by an 11-year-old boy; they raised enough money for Children's to provide free care for all patients for two decades. In 1895, 13 women and two male physicians convened the founding board of the Eye & Ear Hospital.

By the time Davis and her neighbors had launched HLHAS (the Hebrew society), the Homeopathic Hospital's Ladies' Association—Pittsburgh's first permanent volunteer women's hospital auxiliary—had served as a peerless fund-raising machine and a powerful labor force for four decades. Twice weekly, two members inspected the four-story, eight-ward downtown building and its patients. *Should the wards be found in a filthy condition, or the patients unkindly treated, or in any way neglected, you may well imagine that it would not long remain a secret,* declared the hospital's 1870 report.

The ladies consistently met the needs they documented on those inspections. They provided fruits and vegetables from their own gardens, sheets from their own linen closets, and clothing for the infants of unmarried mothers. They found employment for patients without jobs and read the Bible aloud in the wards. And in a time when donors oversaw the dispensation of their beneficence, the Ladies' Association—dominated by members of the Temperance movement—refused to pay for the care of "those who had brought themselves to distress by their own dissipation."

Mary Copley Thaw—a mother of five and wife of Steel City shipping magnate William Thaw—served as chair of the Ladies' Association from 1891 to 1913, ultimately overseeing a campaign that would raise $65,000 for the hospital's 1910 move to Shadyside. In 1918, she sent a memo to the executive committee of the Homeopathic Hospital. "I cannot think why this has never occurred to me before," she wrote, "but I do believe it would be an excellent idea for the hospital to keep chickens."

For three decades, Thaw had seen to the hospital's needs, both large and small. When Elizabeth Rigg Pitcairn supplied an ambulance in 1888, Thaw provided the horses to pull it. She also gave $30,000 for an Eye and Ear Annex to the main hospital, homemade jelly, iron heating stoves and ventilators for the kitchen, a dozen brooms, and a pew in her church for the nurses. She sponsored weekly banjo, guitar, and mandolin recitals "to break the dull routine of hospital life" and in 1910, interviewed and hired a cook for the nurses' dormitory.

Understandably loathe to offend so generous a benefactor, the committee replied that if Thaw were to provide for their housing, it would buy hens. Thaw sent the coops and, for a time, patients at the Homeopathic Hospital enjoyed some of the freshest eggs in town. ■

—Sharon Tregaskis, with reporting by Mary Brignano, author of Inheritors of a Glorious Reality: A History of Shadyside Hospital *and* A Gracious Legacy: Remembering the Ladies' Association of Shadyside Hospital. *Additional resources include Sister M. Cornelius Meerwald's* Mercy Hospital 1847–1959, *Lee Gutkind's* One Children's Place: Inside a Children's Hospital, *and* To Good Health and Life: L'Chaim (A History of Montefiore Hospital of Pittsburgh, Pennsylvania, 1898–1990) *by Samuel P. Granowitz, Lu Donnelly, and Carol Stein Bleier.*





How has medicine changed since the Victorian era? Let us count the ways. Both in Pittsburgh and beyond, Pitt people have advanced how we treat diseases and disorders of the body and brain—from head to toe, inside out, and all the way down to the molecular level. Here are 125 game-changing medical discoveries and technologies (along with a few sundries) from our 125-year history that will blow your bowler back.

THE HUMAN BODY: SEEN FROM HERE

A SHORT LIST OF ESPECIALLY NOTABLE BREAKTHROUGHS IN MEDICINE MADE BY PITT PEOPLE (BOTH AT PITT AND ELSEWHERE) AND SOME OTHER THINGS YOU'LL WANT TO KNOW.

FROM HEAD TO TOE:

1 Discovery of the first biomarker for glaucoma. (J. Schuman, 2001)

2 Promoting stricter surgical criteria for some of the most common operations performed on children, including tonsillectomies, adenoidectomies, and tympanostomy-tube procedures. Perhaps no one has done more for children by showing that less had to be done to them than Pitt's Professor Emeritus of Pediatrics Jack Paradise, whose series of clinical trials helped make this happen.

3 Rewriting the rules on treating head and neck cancer that has spread to the lymph nodes. By adding chemotherapy to the standard post-op regimen of radiation in the 1980s, doctors in Pitt's Department of Otolaryngology found that they could prevent local recurrence and increase survival rates. **4** A decade later, Pitt professor Jennifer Grandis (MD '87, Fel '92, Res '93) discovered that epidermal growth factor receptor is overproduced in tumors from patients with head and neck cancer.

5 The endoscopic endonasal approach for operating on the skull base using minimally invasive tools inserted through the nostrils. Pitt otolaryngologists and neurosurgeons have done more than 2,000 procedures since 1999 for benign and malignant tumors.

6 Demonstrating in 1956 that mouth-to-mouth rescue breathing was superior to then-current methods. To do this, Pitt's Peter Safar (then chief of anesthesiology at Baltimore City Hospital) paralyzed volunteers with curare, then monitored blood-oxygen levels as different methods of artificial respiration were employed.

7 Peter Safar realized that there was little point in saving a heart or lung if the brain was not also protected. He championed the use of mild hypothermia to preserve brain function. The procedure has been recommended by the American Heart Association for use in ventricular fibrillation cardiac arrest patients since 2003. His colleagues at Pitt's Safar Center for Resuscitation Research are about to start trials applying deep hypothermia, now known as emergency preservation and resuscitation, to buy time while traumatic injuries are repaired.

8 The first modern ambulance service. In 1967, Safar worked with Phil Hallen of the Maurice Falk Medical Fund and community leaders to build Freedom House Enterprises Ambulance Service, which trained first-responders from the Hill District.

9 Advancing a novel candidate vaccine for pneumocystis pneumonia, a common illness associated with AIDS and leukemia in children. (J. Kolls, 2005)

10 Isolated and cultivated *Legionella micdadei*, the second bacterial species recognized to cause legionella-based pneumonia. (A.W. Pasculle, 1980)

11 Discovering that serine and matrix metalloproteinases—products of the immune response to cigarette smoke—are at the heart of emphysema and possibly lung cancer. (S. Shapiro, A.M. Houghton, 2008)

12 The pneumonia severity index, considered the best bedside tool to help guide decision-making in patients with pneumonia. (M. Fine, D. Yealy, 1997)

13 Improving paramedic advanced care, especially managing those with circulatory and respiratory failure. (1980 through today)

14 Inventing a technique for correcting deformities of the chest wall. (M. Ravitch, 1950)

15, **16** Changing the outcomes of countless women with breast cancer by improving their chance of survival and quality of life. As a result of almost 50 years of laboratory and clinical research conducted at Pitt, Bernard Fisher (MD '43) dramatically changed our understanding and treatment of breast and other cancers. He showed in 1985 that lumpectomy was just as effective as radical mastectomy, a disfiguring procedure that had been widely used for much of the last century. Fisher was also the first to show that breast cancer is a systemic disease and proved, by clinical trials, the value of systemic therapy following surgery. Other trials by him demonstrated that some breast cancers can be prevented and that preoperative chemotherapy enables more women to have a lumpectomy instead of mastectomy. He is considered the first to promote cancer treatment based on science rather than opinion. **17** Fisher is best known for these breast cancer treatment advances. What most people don't know is that the Pitt Distinguished Professor of Surgery started out as a renal and liver specialist.

18 Discovering that certain breast cancer cells may fail to produce estrogen receptor because of nongenetic mechanisms that contribute to a gene's silencing—i.e., epigenetics. (N.E. Davidson, 1994)

19 Establishing interferon alfa-2b therapy as the first—and to date the only—effective adjuvant medical therapy for prevention of relapse and death from surgically treated melanoma with a high risk of recurrence. (J. Kirkwood, 1995)

20 The first to use activated natural-killer cells to treat advanced melanoma, as well as kidney cancer. (R. Herberman, 1987)

21 The first double-hand transplant in the United States was led by Pitt plastic surgeons in 2009.

22 Making modern vascular surgery possible. Faculty member C.C. Guthrie's early 20th-century work became the basis for future development in the field. **23** Many of Guthrie's experiments wouldn't go over well today, such as "successful transplants of heads, kidneys, and other tissues, alive and preserved, on dogs and other animals."

24 Invention of the sutureless heart valve. This 1964 innovation, which shortened the dangerously long surgery time by an hour, raised valve-replacement survival rates from 10 to 98 percent. (G. Magovern Sr.)

25 Developing exchange transfusion, a lifesaving procedure for newborns with Rh disease (1963). Paul Gaffney (MD '42) performed more than 10,000 during his tenure at Children's.

26 Pennsylvania's first heart transplant, performed by Henry "Hank" Bahnson in 1968 (chair of Pitt's Department of Surgery from 1963 to 1987). Considered one of the finest surgeons and innovators of surgery of his time, Bahnson, while at Johns Hopkins, also was the first to repair aneurysms of the aorta where it arched out of the heart. **27** One of Bahnson's trainees happened to grow up playing with the Bahnson children and recalled some early memories—like how the heart surgeon could cavalierly reach into a horse's mouth to adjust a bit or could rig an automobile engine to pull a rope, towing skiers to the top of the hill behind his house.

28 The authoritative book on comparative coagulation systems, by Pitt researcher and leader of the Central Blood Bank for decades, Jessica Lewis.



Transplant surgeons relied on her knowledge of clotting issues: "I don't think our program here would have gotten off the ground if it hadn't been for her," Thomas Starzl said in her *Pittsburgh Post-Gazette* obituary. **29** Lewis was half of a Pitt husband-and-wife team that changed medicine in Pittsburgh forever. Husband Jack Myers, legendary chair of medicine, was a fabled and exacting diagnostician whose influence on medical education was felt far beyond Pittsburgh. The couple drove to Pitt separately, met at day's end for a cocktail, but had a pact not to discuss each other's work.

30 Confirming in 2000 that diabetic patients who require revascularization fare better with surgery than with angioplasty. This was one of many instances in which Pitt Graduate School of Public Health's Katherine Detre "helped establish the gold standards for determining whether a medical or surgical therapy was good or not so good in spite of opinions of the experts," noted one colleague.

31 One of the first research-oriented pathology programs. Here, in the 1950s, a young up-and-comer named Frank Dixon uncovered the mechanisms of diseases resulting from immune-response misfires, including serum sickness, lupus, and antiglomerular basement membrane disease. **32** Dixon, an MD and one of the first immunopathologists, served as Pitt's pathology chair from 1951 to 1961. Apparently, his passion for the work was infectious—19 members of the Class of '56 alone went into pathology.

33 Seminal studies on the pathogenesis of kernicterus, paving the way for future studies on bilirubin-induced brain injury. (R. Day, 1954)

34 Understanding the role of hepatocyte growth factor, its receptor, and the role of extracellular matrix. (G. Michalopoulos, 1984)

35 Revealing that an antiseizure drug may be able to reverse the clinical effects of a genetic disease—alpha1-antitrypsin deficiency—that is the cardinal genetic disease for which children undergo liver transplantations. (D. Perlmutter, 2010)

36 The world's first liver transplant. (Pitt's Thomas Starzl, in Denver, 1963; he did the first successful one in 1967. His arrival in Pittsburgh in 1981 would mark a defining era in transplant medicine. His team, with others at UPMC and Pitt, would make headlines for years to come. Read on.)

37 The world's first multivisceral transplant. (1983 at Children's Hospital of Pittsburgh of UPMC)

38 The world's first double-transplant operation. (A heart and liver for 6-year-old Stormie Jones in 1984)

39 The world's first pediatric double-lung transplant. (1988)

40 The world's first baboon-to-human liver transplant. (1992)

41 Proving the clinical viability of the immunosuppressants cyclosporin and tacrolimus. (T. Starzl, 1980s) **42** On June 8, 1986, Thomas Starzl and three other Pitt surgeons looked down from 20,000 feet upon the forests of Nova Scotia, where they were going to procure a liver. Suddenly, hydraulic fluid spewed across the plane. They lost the nose gear, plus hydraulic brakes and flaps for deceleration. Starzl's comment: "I always suspected it would end this way." It didn't end that way, of course. Starzl's question on deplaning from the smoking hulk beyond the end of the runway: "How do we get back to Pittsburgh?" A new plane streaked to Halifax from New York while the team procured the organ. Nine hours after leaving, the team returned to Pittsburgh and began the life-saving transplant.

43 The classic textbook *The Body Fluids:*



ILLUSTRATION BY JESSE LENZ

Basic Physiology and Practical Therapeutics. Pitt's prolific Thaddeus Danowski, who developed the pediatric diabetes program at Children's Hospital in 1947, penned 600 scholarly works.

44 Successfully developing synthetic insulin. Panayotis Katsoyannis' five years of toiling in his Pitt lab to decipher the 200 delicate steps in the synthesis process, *LIFE* reported in 1964, "was roughly equivalent to working a dozen jigsaw puzzles simultaneously while blindfolded."

45 Confirming, in 1967, that insulin deficiency distinguished type 1 from type 2 diabetes. (A. Drash) Today, Pitt doctors are identifying the genes and proteins involved in the creation of new insulin-producing cells (A. Stewart); they've developed an innovative experimental vaccine for type 1 diabetes (M. Trucco, N. Giannoukakis); and they've shown that the thymus is arguably just as important for type 1 diabetes development as the pancreas (Y. Fan, M. Trucco).

46 Dispelling the myth that pancreatitis is almost always associated with alcoholism. David Whitcomb identified a number of genetic causes for pancreatitis and proved that all pancreatitis begins with trypsin activation. 47 In 1995, the Pitt prof made one of the most important breakthroughs in pancreatitis research in a century ... by throwing a party. At a reunion hosted for a family that had a rare, genetic form of pancreatitis, the scientist took more than 100 blood samples. The following year he published his groundbreaking finding: The affected family members were genetically predisposed to pancreatitis through autodigestion set off by loss of regulation of the protein-digesting enzyme trypsin.

48, 49 Demonstrating that glomerular failure lies at the root of every renal disease. Pitt grad Barry Brenner (MD '62) also found that antihypertensive drugs lowered glomerular pressure, allowing the kidney to survive longer. 50 Harvard's Brenner is "probably the world's top nephrologist," noted a colleague a few years ago. Yet shortly after his arrival as a new student to Pitt med, Brenner spotted a "super genius" from his high school. Panic washed over him: *My God, how am I going to compete if everyone is at this level?* (The genius from home eventually dropped out of the program.)

51 Discovery of "Compound E," now known as cortisone. Philip Hench (MD '20) and his Mayo Clinic colleague Edward Kendall had a hunch for years before they were able to test it—a hunch that Kendall's newly discovered adrenal hormone, Compound E, might help people with crippling arthritis. But it was a complex compound to create in the lab. The pair waited from 1941 until 1948 before they got a break. Rumors that Germany had been using adrenal hormones to give their fighter pilots an edge spurred U.S. military support for synthetic-hormone research. For cortisone work and related studies, Hench and Kendall won the 1950 Nobel Prize in Physiology or Medicine. 52 The mysteries of medicine weren't enough to satisfy Hench's fecund mind: A Sherlock Holmes devotee, Hench amassed a collection of first editions and related materials that came to be included in the Special Collections and Rare Books Department at the University of Minnesota.

53, 54 Pioneering the use of titanium and other durable materials in hip and knee replacements. Also: the medial open reduction technique to correct dislocated hips in infants resulting from breech birth. (A. Ferguson, 1950s)

55, 56, 57 Pitt orthopods have managed other feats that became the foundation for the future of cartilage science and repair, including: showing that injection of cortisol could harm cartilage (1966); leading the development of cartilage tissue engineering (1970); and the first recorded successful cartilage cell joint allografts (2000).

THE BRAIN (AND NERVOUS SYSTEM)

SOME OF THE MOST SIGNIFICANT ADVANCES TO COME OUT OF PITT PEOPLE'S UNDERSTANDING OF OUR SYNAPTIC CONNECTIONS. OUR COUNTDOWN CONTINUES.

58 ***The Common Sense Book of Baby and Child Care*** **(1946). Benjamin Spock's bestselling treatise, rooted in a study of psychoanalysis that encouraged parents to trust their instincts (noting, for example, that it's okay to show affection), redefined parenting. Spock brought to Pitt pediatrics an emphasis on child development rather than childhood illness. 59 After World War II, Spock's book seemed to be at every cribside, soothing anxious parents. In the turbulent '60s he built a different reputation—as an outspoken opponent of the Vietnam War and the military draft in particular. Arrested for allegedly counseling young men to disobey the draft law (charges were later dropped), he ran for president (1972) and then vice president (1976). (In 1967, he was slated to be named Martin Luther King Jr.'s vice-presidential candidate at a conference reportedly disrupted by "government** ***agents provocateurs***.**")**

60 One of the first psychiatry departments to insist on evidence-based medicine. Thomas Detre arrived in 1973 to take the reins of Western Psychiatric Institute and Clinic (WPIC) and the Department of Psychiatry. From the get-go, Detre saw rigorously researched medicine as the future of his field—with psychiatrists partnering with biologists, neurologists, epidemiologists, geneticists, and others. He was one of the people most responsible for propelling Pitt to the top tier of medical schools and for making UPMC what it is today.

61 Uncovering biologically based root causes of mood disorders and better detection methods and long-term treatment strategies. (D. Kupfer, 1990s)

62 Revealing the relationship of sleep disorders to cardiovascular health, depression, and menopause. (D. Kupfer, starting in 2000)

63 Chairing the task force charged with revising the forthcoming fifth iteration of the ***Diagnostic and Statistical Manual of Mental Disorders (DSM)***, **the bible of psychiatry. That would also be David Kupfer, a Thomas Detre protégé. By promoting evidence-based collaborations between clinical- and basic-science investigators as chair of the psychiatry department from 1983 to 2009, Kupfer has made WPIC one of the preeminent university-based psychiatric centers, with an encyclopedic roster of psychiatric-disorder studies.**

64 The recent finding that GABA neurons, which regulate working memory, function improperly in people with schizophrenia. The abnormality represents a promising molecular target for treating cognitive impairment in those with the disorder. The same team has identified a compound that boosts GABA-neuron signaling. (D. Lewis, 2004, 2008)

65 Tracing signals in the brain using viruses to discover, for example, that learned movement, such as a master pianist's performance of a concerto, follows a route from cortex to cerebellum to the ivories. Peter Strick's work has contributed greatly to our insights on how the brain operates as a network—most notably, that the cerebellum and the cerebral cortex continuously exchange information in a closed-loop circuit, and that the human cerebellum is well connected to higher-brain centers. 66 As befits someone who was a high school basketball teammate of baseball legend Reggie Jackson, Distinguished Professor of Neurobiology and codirector of the Center for the Neural Basis of Cognition, Pitt's Strick, retains a passion for athletics and what it illustrates about human actions, especially automatic movement.

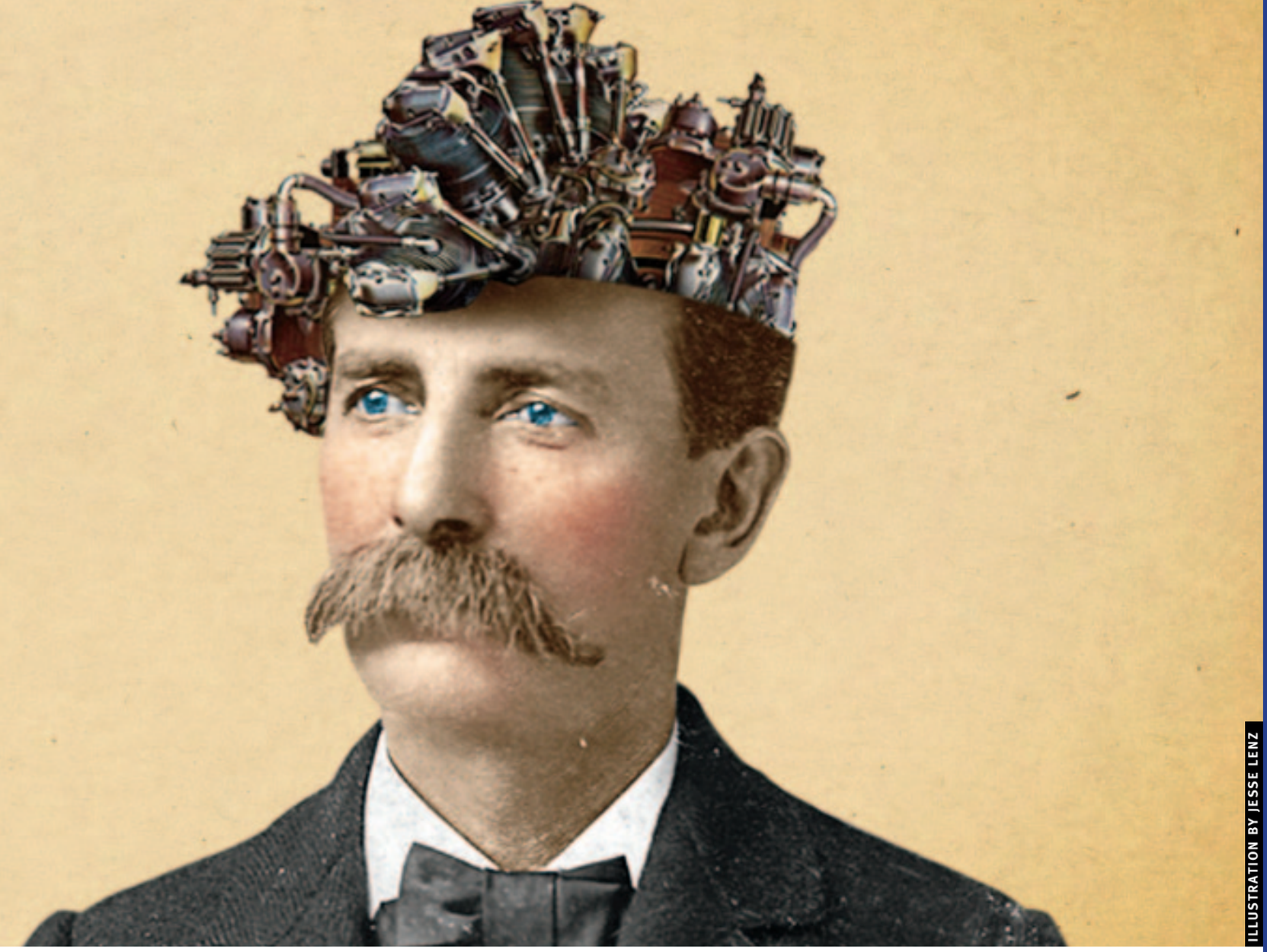


ILLUSTRATION BY JESSE LENZ

67 Building an understanding of neuronal communication, as well as the required cyborg technology, to allow an otherwise immobile person to move a robotic arm just by thinking about it. (A. Schwartz, starting in 1988)

68 Discovering, in the 1960s and 1970s, the neurological mechanism of urination—from the primitive reflex in infancy to the voluntary control we develop as toddlers—as well as how the bladder's network of nerves rewires itself in the wake of a spinal cord injury. **69** Disorders of the sacral nerves, which control the autonomic functions of the bladder, bowel, and reproductive organs, have always been shrouded in shame. Treatment lagged behind other neurological conditions because so little was understood about the unique wiring at the base of the spinal cord—that is, until Distinguished Professor of Pharmacology and Chemical Biology William "Chet" de Groat brought these diseases out of the water closet.

70 Pittsburgh Compound B—the first noninvasive method of detecting beta-amyloid proteins that form the plaques in the brain tissue of people with Alzheimer's disease. **71** Pitt psychiatrist William Klunk and radiochemist Chester Mathis have been fishing buddies for years. Between them, they've caught trout, steelhead, salmon, and even each other (with the rare errant cast) on their many expeditions along the streams of Lakes Erie and Ontario. But there's a reason it's called "fishing," not "catching"—it takes patience, something these scientists are no strangers to. Klunk and Mathis tried hundreds of compounds over almost a decade before successfully developing the radiopharmaceutical dye known as Pittsburgh Compound B at Pitt in 2002.

72 Outing the dangers of even low-level lead exposure, including lower IQ and shifts in behavior that lead to delinquency. Herbert Needleman's studies were key in persuading the Environmental Protection Agency to take lead out of gasoline in the 1970s, making possible a 90 percent reduction in blood lead levels in American children. **73** As a self-admittedly cocky young resident in Philadelphia, Needleman (who would later do his important lead-exposure work as a member of the Departments of Pediatrics and Psychiatry at Pitt) brought a little girl with severe lead poisoning back from a coma, breathed a sigh of relief, and told the girl's mother she'd make it—they'd just have to move out of that lead-paint-infested home. Angry, the mother snapped. *Where can I go? Any house I can afford will be no different from the house I live in now.* Needleman realized lead itself wasn't the problem—it was the society that had allowed her to live in a toxic environment simply because she came from a low-income family.

74 The discovery, in 1949, of Riley-Day syndrome, a disorder of the autonomic nervous system. **75** When Richard Lawrence Day—Pitt's chair of pediatrics from 1960 to 1965—was 80 years old, he accidentally left a spoon in the freezer, and when he removed it, he dropped it into a cup of hot water he had heated in the microwave. The water immediately began to boil. Intrigued, Day studied the phenomenon with the help of a Yale engineer and wrote a detailed, erudite explanation that was published in a letter to *Nature*.



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THE CELL (AND MOLECULES)

PITT MEDERS SHOW THAT MICROSCOPIC THINGS MEAN A LOT. OUR COUNTDOWN CONTINUES.

76, 77, 78, 79 Offering a mathematical means for determining the rate of an enzyme reaction. Maud Menten accomplished this in Berlin with Leonor Michaelis. After arriving at Pitt in 1923 as an assistant professor of pathology, Menten discovered the azo-dye coupling reaction for alkaline phosphatase (which is used as a dye in histology), characterized several bacterial toxins, and conducted the first electrophoretic separation of proteins in 1944. (She also investigated the properties of hemoglobin, the regulation of blood sugar levels, and kidney function.) That's some of it. Menten was a clarinetist, an exhibited painter, a polyglot, and a stickler for doing English tea time properly.

80 Creating a technique in 1952 that allowed the poliovirus to be produced in adequate quantities for use in the Pitt team's successful vaccine.

81 Julius Youngner, the Pitt virologist alluded to above (who is now Distinguished Service Professor Emeritus), also figured out how to culture cells derived from animal tissue, forming the foundation of modern cell culturing. (1947) **82** When in the army and stationed at Oak Ridge, Tenn., during the Manhattan Project, a civilian worker asked Youngner what was going on. He had no idea, actually, but couldn't resist yanking the man's chain. Drawing himself up to appear as in-the-know as possible, Youngner looked the gent in the eye and asked, ominously: "Do you want to get in real trouble?"

83 Describing plasma protein metabolism in children with kidney disease. (D. Gitlin, 1952)

84 Unraveling the process of intestinal iron absorption. (D. Gitlin, 1962)

85 Identifying alpha fetoprotein as a critical indicator of potentially life-threatening birth defects in the developing baby (1967) and ceruloplasmin deficiency as a marker for Wilson's disease (1952). Certain elements of David Gitlin's (the late professor of pediatrics) research required human breast milk. He assigned student Bertram Lubin (MD '64) to do the collecting. "I felt like Clarabelle Cow," Lubin says with a laugh.

86 Proving that our bodies produce nitric oxide and mapping out its biochemical pathway. A Pitt med grad's work in immunology helped to unravel this entirely new principle for signaling in animals. The University of Utah's John Hibbs Jr. (MD '63) pursued his studies at the same time as others who later won the Nobel Prize in Medicine or Physiology for similar findings in the cardiovascular system.
87 Pitt faculty members are moving nitric oxide breakthroughs from the bench to the bedside: In clinical studies, they are using the pathway to protect the liver from damage. They're also testing ways to remove excess nitric oxide in cases of shock.

88 A Pitt med grad figured out that hormones control certain genes, was the first to isolate a hormone-regulated gene, and cloned it (showing it was possible to reproduce genes). 89 The same grad, Bert O'Malley (MD '63), also uncovered how receptors, and therefore the genes they regulate, turn on and off, and he introduced the endocrine world to molecules called "co-activators," which regulate gene expression. 90 In the creation story of his research career, which came first for Bert O'Malley, Father of Molecular Endocrinology, the chicken or the egg? Answer: Neither. Er, both. Well, actually, it was the oviduct, the passage from the hen's ovaries to the outside, which undergoes dramatic changes in response to estrogen. O'Malley recognized that this system would be ideal for a series of hormone studies when he was working for the National Institutes of Health in the 1960s.

91 Discovery of a new category of lymphocytes called natural-killer (NK) cells. (R. Herberman, 1975)

92 Elucidating the DNA-repair process. The process can be likened to the work of a road crew finding a pothole in a highway, assessing the damage, and filling the hole. In the past decade, Pitt has built an impressive braintrust in this area. (The dean himself has an active lab.) One Pitt investigator appended quantum dots to DNA-repair proteins and became the first to watch multiple repair proteins in action. (B. Van Houten, 2009) Another realized that ATM kinase, a biochemical catalyst, is vital for the survival of cancer cells; it allows them to repair their DNA. By inhibiting ATM activity it's possible to selectively kill cancer cells that experience replication stress as a consequence of somatic mutation. (C. Bakkenist, 2010)

93 Stablizing a cancer stem cell line. Ephemeral by nature, transforming quickly into mature cancer cells, cancer stem cells are difficult to study in their stem cell state. Or at least they were until a Pitt prof recently managed to freeze them in time. (E. Prochownik, 2010)

94 Identifying two of the seven known human cancer-causing viruses: KSHV (1993), which causes Kaposi's sarcoma, and MCV (2008), the suspected culprit in the majority of cases of Merkel cell carcinoma. (Y. Chang, P. Moore)

95 Numerous seminal contributions to our understanding of "unorthodox" DNA structures and how they can lead to mutation. Fresh out of Pitt med's PhD program, biochemist Robert Wells (PhD '64) turned down a faculty gig at Princeton on a hunch that another offer—a fellowship at the University of Wisconsin with H. Gobind Khorana—was the ticket. This turned out to be one honey of a hunch: Within two years, the group had cracked the genetic code. (Khorana received a Nobel in 1968.) Wells has since led a number of notable organizations, including the Center for Genome Research at Texas A&M.

96 Synthesizing adrenocorticotrophic hormone, which helps preserve critical brain function during physiological stress or trauma. Klaus Hofmann managed to do this in 1961, when chair of the Department of Biochemistry.
97 As one of Hofmann's grad students, Robert Wells experienced some stress while running an experiment that literally blew up in his face. In the wake of the accident, Hofmann calmly told Wells, "Bobs, I think you better take the rest of the day off."

98 The first evidence that a heart defect is genetically linked to a dysfunction in cilia. (C. Lo, 2007)

99 Showing that there's order to necrosis, thought to be a chaotic and irreversible process, by finding that it's actually a response to stress regulated by a protein called a serpin. (C. Luke, G. Silverman, 2007)

100 Pinpointing in 2009 an enzyme inhibitor that allowed for a deeper understanding of the role of the fibroblast growth factor pathway in heart development and wound healing. With this knowledge, Pitt's Michael Tsang even managed to enlarge a developing heart.

PESTILENCE

A VERY BRIEF RECAP OF PROFOUND ADVANCES IN INFECTIOUS DISEASE MADE BY PITT PEOPLE.

101 Halting the spread of polio in America and elsewhere with the development of the killed-virus polio vaccine. (Pitt polio team, 1955)

102 Leading the effort to eradicate smallpox worldwide. (D.A. Henderson, 1966–1977)

103 Creating the Jerne plaque assay, a popular test for visualizing and counting antibody-producing cells that revolutionized immunology research and was used for many years. (N.K. Jerne, 1963)

104 The natural selection theory of immunology (1955), which asserts that all kinds of specific, original antibodies (these came to be known as products of lymphocytes) already exist in an organism, pre-formed, ready to fight off intruders. Before this idea took hold, scientists believed that viruses and other antigens somehow "instructed" the immune system to build original, appropriate antibodies. 105 Pitt prof Niels Jerne's Darwinian take on immunology—which began percolating in Copenhagen while he was doing MD dissertation work in a lab shared with a young James Watson (who was working on another project)—held him up as one of biology's great theoreticians and won him a Nobel. But it took years to convince people. When Jerne secured an audience with Linus Pauling to describe his idea, Pauling took it in, understanding it completely within minutes. Then he dismissed it entirely. When Jerne met up with Watson years later at one of Pasadena's all-night eateries, he asked him what he thought of the theory. Watson was succinct: "It stinks!"

106 Determining that viral loads, not just T-cell counts, matter in assessing who with HIV is likely to develop AIDS. The same Pitt med team, led by John Mellors, also contributed to the first long-term effective antiretroviral therapy and took on the puzzle of HIV resistance to antiretroviral drugs. These advances were made possible by the Graduate School of Public Health's Pitt Men's Study. Founded in 1983 by Charles Rinaldo, the study investigates the natural history of AIDS in more than 3,000 homosexual men in Pittsburgh. As part of a national effort, the research has allowed scientists to learn how the virus spread, discover ways of measuring the disease's progression, and find interventions that help HIV-positive people live longer.
107 The *Pittsburgh Post-Gazette* reported that club-owner involvement was a unique part of the Pitt Men's Study. Tavern Guild members even tried to convince bar and bathhouse owners in other cities to distribute AIDS information and condoms. A Philadelphia gay bar owner asked one Pittsburgh club owner why he'd want to chase away business by reminding people about the virus. He responded, "When people die, they don't buy any drinks at all. They're not ever coming back."



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YOU DID *THAT*?

HERE'S TO THE CREATIVITY OF PITT PEOPLE THAT MAKES US HEALTHIER. WE END OUR COUNT WITH ANOTHER SHORT LIST.

108 Robert Egan (MD '50) spent the early part of his career using inanimate objects as well as human subjects to find the perfect positioning of the breast for X-rays by trying everything from compressing the breasts to "floating" them in liquid. The "Egan technique" caught on and became the basis for modern mammography.

109 Mark Ravitch, who for 20 years was a Pitt professor of surgery, helped to introduce mechanical suturing techniques in the United States after seeing surgical staples used on a 1958 trip to Russia.

110 Biochemist Herbert Boyer (Arts & Sciences PhD '63) and geneticist Stanley Cohen first met at a conference in Hawaii in 1972. Afterward, over hot pastrami and corned beef sandwiches, they cooked up a way to genetically engineer cells to produce biological chemicals. Boyer and Cohen's first successful attempt at gene splicing, or recombinant DNA, followed a few months later.

111 Fellow Pitt undergraduate alum Paul Lauterbur (A&S '62) is further evidence that the best way to the heart of discovery may well be through the stomach. His *aha!* moment came in 1971, mid-bite into a Big Boy burger. Lauterbur won a Nobel Prize in Physiology or Medicine for a concept that took shape that day in his scribbling on, yes, a napkin: magnetic resonance imaging (MRI).

112 The liver is a big bleeder. When Thomas Starzl was perfecting liver transplantation, docs had to hand pump unit after unit of blood. John Sassano (Res '80) found a way around the problem by inventing the rapid infusion pump, which has become standard equipment in ERs and ORs.

113 In 1985, a Pittsburgher named Tom Gaidosh received an artificial heart, and then, a few days later, a heart transplant. His was the world's second implant of the device as a bridge to transplant, and the first successful one—he lived for 12 more years. Both surgeries were performed at UPMC by Bartley Griffith (Res '81, Fel '78).

114 L. Dade Lunsford at the Center for Image-Guided Neurosurgery at Pitt used the first Gamma Knife in North America in 1987.

115 While at Johns Hopkins University in 1988, Pitt's Jeremy Berg predicted the structure of "zinc fingers," which slide into the DNA double helix at precise positions. Research scientists now design custom zinc finger proteins to recognize genetic sequences they want to exchange in "knock-out" animal models.

116 The Peter M. Winter Institute for Simulation Education and Research (WISER) opened its doors in 1994. The idea was pretty simple: Give students a chance to train in a real-world environment without putting a patient at risk. What they built became the world's most widely used patient simulation center.

117 Former WISER directors created a respiratory simulator called AirMan, some of whose technology was later licensed to the company that developed SimMan (a multi-purpose, computer-run simulator) and SimBaby. There are now 4,000 Simfolk helping to train medical personnel the world over.

118 On the top floor of Pitt's Scaife Hall is the Emergency Medicine Communication Center that fields calls from commercial airlines, Pittsburgh Medic Command, and STAT MedEvac, the largest private air medicine service in the country (with the second busiest heliport after the Pentagon).

119 A Pitt prof developed fluorescence light microscopy instruments and reagents, giving scientists a new perspective on living cells. D. Lansing Taylor created his first such image using a newly declassified military night-vision camera in 1974.

120 Optical coherence tomography, a 3-D optical biopsy that can catch signs of many types of eye disease before vision loss sets in, was patented by Pitt's Joel Schuman in 1994.

121 Among Bert O'Malley's (MD '63) many patents is a switch to turn genes off and on in humans and other animals.

122 About 11 percent of U.S. hospitals use basic electronic medical records. UPMC is among them—and has been for more than 20 years, thanks to a Pitt prof. In 1989, John Vries developed the Medical Archival System (MARS), one of the first such systems in the country.

123 Managing digital radiology images once required huge, centralized systems. That is until a Pitt radiologist created the Stentor system, which leverages less-expensive PCs and the World Wide Web. (P. Chang, 1998)

124 The average wheelchair user will push his hand rims perhaps 3,000 times a day. So Pitt researchers developed the Natural-Fit, a best-selling ergonomic hand rim that has helped tens of thousands of wheelchair users see the light at the end of the carpal tunnel.

125 Pathologists are able to make evaluations accurately from remote sites thanks to work done by clever folks here. Pitt docs are among the first to take thousands of digitized pathology images and quilt them together via software. They can use these images with integrated clinical data to make pathological diagnoses. ■

BY THE NUMBERS

AND SINCE WE'RE IN THE COUNTING MOOD, WE'LL SIGN OFF WITH THESE NOTABLE NUMERICS.

In its 125 years, the School of Medicine has minted 10,671 MDs.

Twenty-two men made up the first faculty of the medical college. The School of Medicine now has more than 2,000 regular faculty members (38 percent of whom are women), plus an additional 2,098 volunteer faculty.

All six women holding permanent department chairs in the medical school, the only women to do so in the school's history, were appointed in the past 13 years during Arthur S. Levine's tenure as dean.

Eleven-year-old Kirk LeMoyne inspired the founding of a hospital for children in Pittsburgh. In 1883, he formed the "cot club" which sponsored "the baby show," a beauty pageant for children. The first effort raised $3,000 and led to other fundraisers that planted the seeds for Children's Hospital of Pittsburgh.

Two hundred and ninety-eight children visited Children's Hospital as outpatients in 1896, and 213 were admitted, mostly "foundlings" left on its doorstep.

It's been said that the clinical trial of the polio vaccine—involving 1.8 million children across 12 states—could not be done today. (Add this to your list of things that wouldn't fly today: Pitt medical students were encouraged to roll up their sleeves for the double-blind trial of the vaccine.)

Since 1997, the University of Pittsburgh (with its affiliates) has been one of the top 10 National Institutes of Health–funded institutions.

The School of Medicine can count four recipients of the Presidential Early Career Award for Scientists and Engineers among its ranks. The award, started by President Bill Clinton in 1996, is the government's highest honor for young scientists.

Pitt has the busiest postcardiac-arrest service in the nation. Since 2007, the service has assisted in the care of patients at UPMC Presbyterian and includes the therapeutic use of hypothermia. Thus far, its team has seen 443 patients.

The Department of Psychiatry has ranked number one in NIH funding among all such departments since 1987.

For 2009, the School of Medicine received 5,202 applications. The incoming class consisted of 150 students.

Seventeen School of Medicine faculty members are among the 1,649 members of the Institute of Medicine. Four have been elected to the National Academy of Sciences, which votes in just 72 U.S. scientists each year.

Pitt med students learn the basics of clinical practice from 92 standardized patients, who range in age from 18 to 77.

Pitt's 10,000-tank zebra fish facility can accommodate up to half a million fish for research models.

The class entering the school in 1908 had 145 members, of whom 60 graduated and 40 passed the state-licensing exam.

The Class of 2008 was the first to complete the scholarly project, which was introduced to the curriculum in 2004. Their work resulted in 13 fellowships, grants, or other national awards; 20 School of Medicine awards; co-authorship of 42 peer-reviewed papers; and more than 46 national presentations and abstracts. (Harvard Medical School just announced it will require a similar scholarly project of all of its medical students.)

Bling! After their Super Bowl XLIII victory, the Pittsburgh Steelers had a championship ring fashioned for Robin West (Fel '03), Pitt associate professor of orthopaedic surgery and the team's assistant orthopaedic surgeon. The ring joined her Super Bowl XL pendant.

When *Rolling Stone* magazine ranked "The 100 People Who Are Changing America," a Pitt scientist checked in at 32. Alan Russell, a PhD professor of surgery and former director of the McGowan Institute for Regenerative Medicine, was described as "a medical futurist who is finding ways for the body to rebuild itself."

At 3 a.m. on Monday, April 27, 2009, the Class of 2009 successfully closed down Forbes Avenue in front of the Original Hotdog Shop to film 72 med students performing a Bollywood-style dance scene for *Scutdoc Millionerrs*. (You've gotta Google this one!)

Even if residents aren't getting a lot of shut-eye, someone usually is on campus. The University's Human Chronobiology Research Program observed 863 overnight studies in just 365 days last year. With that, we'll rest. ■

125TH ANNIVERSARY FEATURE CONTRIBUTORS

Much of the historic section, "The Ills to Which Flesh Is Heir," was written by Barbara I. Paull or is from her book, *A Century of Medical Excellence: The History of the University of Pittsburgh School of Medicine* (1986). Our feature contributors also include Erica Lloyd, Edwin Kiester Jr., Joe Miksch, Chuck Staresinic, Sharon Tregaskis, and Elaine Vitone, with reporting by Mary Brignano, Marc Melada, and Alexis Wnuk.

Sources include Pitt's Archives Service Center, Robert C. Alberts' *Pitt: The Story of the University of Pittsburgh 1787-1987* (1986), Mary Brignano's *Beyond the Bounds: A History of UPMC* (2009), Ruth C. Maszkiewicz's *Presbyterian Hospital of Pittsburgh: From its Founding to Affiliation with the University of Pittsburgh* (1978), David M. Oshinsky's *Polio: An American Story* (2006), Pitt's Office of Public Affairs' *Blue Gold & Black* (2008 and 2010) and *Defeat of an Enemy* (2005), Peter Safar's *Careers in Anesthesiology; An Autobiographical Memoir, Volume V: Peter Safar* (2000), Thomas Starzl's *The Puzzle People: Memoirs of a Transplant Surgeon* (1992), many stories from past issues of this magazine, as well as publications we note on p. 23.



ABOVE: Officials from the University of Pittsburgh and Tsinghua University met in Beijing in April to ratify an agreement that makes two years in Pittsburgh part of the biomedical research training of Tsinghua students. RIGHT PAGE: Shi and Levine sign the agreement.

BEIJING IN PITTSBURGH

CHINA'S CREAM-OF-THE-CROP PHYSICIAN-SCIENTISTS WILL TRAIN HERE

STORY BY MAUREEN PASSMORE

Q & A BY ERICA LLOYD

A few months ago, Yigong Shi felt that his university was missing something. As dean of Beijing's prestigious Tsinghua University's School of Life Sciences, Shi, a PhD, was searching for a U.S. school to send Tsinghua medical students to for biomedical research experience. Meanwhile, the University of Pittsburgh's Arthur S. Levine, an MD, senior vice chancellor for the health sciences and dean, School of Medicine, had been traveling to China in an effort to build relationships with universities there. This was unfolding while Jeremy Berg was about to step down as director of the National Institute of General Medical Sciences to accept a senior position at Pitt. Berg knew both men and, sensing an extraordinary opportunity, introduced them.

Levine and Shi met in Beijing, and, though he had a couple of other high-profile U.S. universities interested, Shi chose the University of Pittsburgh for the unique collaboration. Beginning in the summer of 2012, 25 to 45 Tsinghua medical and graduate students each year will travel to the University of Pittsburgh to enter a two-year biomedical training and research program at the medical school. The two years the medical students spend at Pitt will complement the six years of training they'll receive in China. In addition, the two universities will take turns hosting an annual symposium featuring researchers from both institutions.

A big deal? Simply put, yes. Here's why: Tsinghua is highly regarded for its top science and engineering programs. It has produced one-fourth of the members of the Chinese Academy of Sciences and many prominent leaders in China, including Hu Jintao, China's current president. Shi, himself, is a celebrated structural biologist, renowned for discovering a novel path in cancer treatment. He is also what the Chinese call a "sea turtle"—part of a wave of Chinese professionals who gave up prominent positions abroad to return home. In 2008, while he was professor of molecular biology at Princeton University and after an 18-year residence in the United States, Shi surprised the science community when he turned down a $10 million Howard Hughes Medical Institute investigatorship and resigned from Princeton to return to Tsinghua, his alma mater. (Shi earned his undergraduate degrees in biology and mathematics there.) After careful consideration, Shi chose to partner with Pitt. Levine considers it a win-win, noting, "Our medical school is almost unique among U.S. medical schools for the extraordinary growth and visibility we've had in a short period of time. The advantage for Tsinghua students coming to Pitt is that they will become immersed in a peer-reviewed research culture to complement their medical studies. And, we're adding to our lab workforce medical students who are the best-of-the-best from a country of almost 1.4 billion people and who will, undoubtedly, become leaders of medicine and biomedical research in China. They, presumably, will have a good experience in Pittsburgh, and that will create a durable and important relationship."

Shi knew Berg (who is now Pitt's associate senior vice chancellor for science strategy and planning) from his grad school days. He received his PhD in molecular biophysics from Johns Hopkins University, where Berg was his thesis advisor; and he was eager for Tsinghua students to share the experience and opportunities he had with a U.S. education. Now, in a sense, Tsinghua students will share Shi's mentor, as well—Berg will oversee the program at Pitt.

Recently Dean Shi shared with us his perspective on the partnership and on medicine and science education in both countries.

PITT MED: The United States faces a dearth of physician-scientists. Can you talk a bit about the importance of graduating more physician-scientists in China?

YIGONG SHI: China has seven million physicians, of whom two million have received reasonable training and are providing quality health care to the majority of China's 1.35 billion people. However, China has a severe shortage of physician-scientists. Compared to the U.S., the situation is much direr.

Why this partnership? Why Pitt?

The medical school at the University of Pittsburgh is exceedingly strong in basic biomedical and translational research. The affiliated hospitals are first rate in the U.S. and perhaps in the world. In addition, the size of the medical community at Pitt is large enough to accommodate our students. Last, but not least, I have been favorably impressed by the vision and leadership of Dr. Levine.

You've spoken of modernizing Tsinghua's teaching philosophy. What did you mean?

The traditional teaching method in China emphasizes passive listening and memorization. Students seldom raise critical questions and comments. I have been advocating for active learning in the classroom (engagement between teachers and students, small class size, active discussion groups, student presentations, research-based learning, etc.) ever since I returned to China.

You are a product of both the American and Chinese educational systems. What do you see as the strengths and weaknesses of each?

The strength of the Chinese educational system is clear: Students receive comprehensive and sound knowledge in mathematics and natural sciences. The weakness is also evident: The system does not encourage innovation!

In the United States, it is quite the opposite: Innovation is encouraged by the educational system, but students are only exposed to shallow training in mathematics and natural sciences.

Faculty members here are excited to work with students from Tsinghua. What might they learn from them?

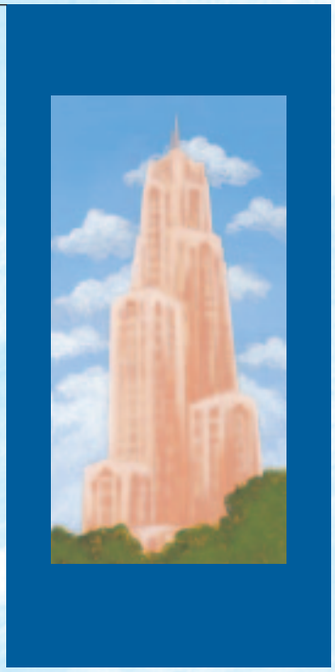
They will be impressed by the overall "raw" quality of the students. But these students need to be carefully crafted before they can be truly "useful" to our society.

As one of China's "sea turtles," how has the experience been for you and your family?

So far, so good. I am physically and mentally exhausted in China, much more so than in the U.S. But I am happy and enormously enjoy what I am doing for my home country. ■



COURTESY TSINGHUA UNIVERSITY



CLASS NOTES

'50s

In 1966, when newly minted Markle Scholar in Academic Medicine **Thomas Piemme** (MD '58) attended his first meeting of the Markles, he heard the term physician assistant (PA) for the first time. He was intrigued. "A lot of what a physician does, doesn't require a physician," the former Pitt assistant chief of medicine (1966–1970) says with a laugh. "The idea of a trained person who could assist the physician—in taking a history, doing a physical, entering orders, doing procedures [putting in an IV line, for example]—made great sense to me." In 1972, Piemme launched a PA training program at George Washington University, then one of only a handful of its kind. Today there are 156 programs and more than 80,000 practicing PAs—who are helping to cover the staffing shortage caused by the 80-hour workweek limit for residents, Piemme notes. He played a key role in establishing the National Commission on Certification of Physician Assistants. He's now coauthoring a history of the rise of PAs.

'70s

As a geriatric specialist, **Judith Black** (MD '74, Geriatric Fellow '87) has seen that, all too often, patients' wishes regarding end-of-life care aren't made clear to their family members. For decades, Black, clinical associate professor of medicine at Pitt and medical director for senior markets at Highmark, has been working with Pitt's Robert Arnold, the Leo H. Criep Professor of Patient Care and professor of medicine, on advance-care-planning. They've pursued various projects, including cofounding the Coalition for Quality End-of-Life Care. Black also led an effort called POLST (Pennsylvania Orders for Life-Sustaining Treatment), which produced a form that turns patients' treatment wishes into medical orders. In October 2010, Black saw a dream realized when POLST was adopted by the Commonwealth of Pennsylvania.

Dennis English (MD '76), vice president of medical affairs at Magee-Womens Hospital of UPMC, and his wife, Denise English, a Pittsburgh physical therapist, have led several teams to remote Haiti. Through the years, Dennis English, an ob/gyn, has taught midwives and nurses patient care, and the teams he has traveled with built homes and schools and established a medical clinic in Lacroix, Haiti. Helping to build self-sustaining medical resources in these areas has yielded "tremendous Haitian support," he says. Back at Magee, Dennis English helped establish the Dan Berger Cord Blood Program.

In **Jerry Collins'** (Pharmacology PhD '79) field, the research is just beginning to scratch the surface. He studies the largely misunderstood neurophysiological mechanisms of itch and its behavioral responses—a strange research interest, it may seem to some. However, "the reality is that itch is a profound clinical problem that a lot of people don't hear about," Collins says. "There's a fair overlap between the sensation of pain and the sensation of itch. The fibers may, in fact, be the same, and there may even be cross-talk between some of the systems so one can be interpreted as the other," he adds. Collins is a professor of anesthesiology at Yale University. He is also a consultant for the National Institutes of Health Office of Laboratory Animal Welfare. In that role he educates the research community about regulations regarding the ethical treatment of lab animals.

'80s

On **Ann McGaffey's** (Family Medicine Resident '83) desk is a photo of her after a rugby match, her nose bleeding, her forehead bandaged. She's brave in her day job, too, where she focuses on childhood health literacy, including obesity prevention and (gulp) sex education.

In 2007, McGaffey collaborated with Kristin Hughes, associate professor in Carnegie Mellon University's School of Design, who created Fitwits (www.fitwits.org), an interactive online tool that uses games and imaginative characters (McGaffey's favorite is "Elvis Pretzley") to make health ed fun. In East End schools and at Bloomfield-Garfield Family Health Center, where McGaffey is medical director, she's using Fitwits to teach kids about nutrition, portion control, and healthy cooking, as well as the birds and the bees. The project has been instrumental in improving the dialogue between

PETER ELLIS: LESS IS MORE

There's an awful lot of duplication in cancer treatments. For metastatic lung cancer alone, there are 38 distinct recommended chemotherapy regimens. How on Earth is a doc to know which to choose for a given patient?

"We said, 'Boy, we could really do ourselves a favor if we narrowed that down to the most effective regimens,'" says Peter Ellis (MD '85), director of the medical oncology network for UPMC Cancer Centers and associate professor of medicine at Pitt. "'And if there's more than one most-effective regimen, let's pick the one that's the least toxic to the patient. And if there are multiple most-effective, least-toxic regimens, let's pick the one that's most cost effective—for the patient, for the cancer center, and for society.'"

That, in a nutshell, is the idea behind Via Oncology, a new subsidiary of UPMC. Since 2004, Ellis has led a team at UPMC Cancer Centers in a massive effort to arrive at the ideal "pathway"—the surest, most tolerable, and least costly option—for every state and every stage of disease, and did this for 13 separate diseases. Each pathway was determined by a committee of disease-specific expert physicians, which was co-chaired by a community clinician and physician-scientist. All of UPMC's 110 oncologists were invited to join in on the effort to comb through the literature for the strategies that would best fit each unique

MARY JANE BENT

doctors and patients on this formidable subject matter, McGaffey reports.



MEGAN MCGREEVY

LAISSEZ LES BON TEMPS ROULER!
As part of Alumni Weekend 2011, the Class of 1961 boarded Pittsburgh's *RiverQuest* for a private cruise and a concert by Dixie Doc and the Pittsburgh Dixieland All Stars. Unfortunately, because of strong currents, the boat never left the dock, but the Doc (a.k.a. Richard Paul, MD '61—that's him on the cornet) and his crew still made a splash. Catch an encore at the Allegheny Elks Lodge on Pittsburgh's North Side, where they play once a month (schedule at www.dixiedoc.com).

'90s

Cervical cancer is far more prevalent in the developing world than in the United States. The hospital in Tegucigalpa, Honduras, for example, treats 60 cases a day. Among these, many are curable, but unfortunately, surgeons who are trained to treat them are in very short supply. Many follow career opportunities abroad, not only because they can make a better living, but because they are frustrated by the lack of technology at their disposal, says **Frederic Price** (Obstetrics and Gynecology Resident '90). "You can try to solve this problem by sending all the money and equipment you want, but if there's no trained manpower, it's not going to work." Price, chair of the Society of Gynecologic Oncologists International Network, has organized a training program for surgical residents in Tegucigalpa. To date, he has made six trips there. He plans to launch a similar program in Ethiopia this December. "We're trying to train indigenous doctors in the hopes that they will stay and work to solve the problems in their own country," he says.



Price (right) with colleague Linus Chang of New York in Honduras.

Throughout his career, **Steven Roy Daviss** (Psychiatry Resident '93) has worked to educate people about psychiatry. "I do often get a sense that people, even other physicians and health professionals, don't really understand it," says Daviss, chair of psychiatry at Baltimore Washington Medical Center and a clinical assistant professor at the University of Maryland School of Medicine. "It's not Hannibal Lecter, and it's not Frasier Crane, and all the media images that people have." Recently, Daviss and two of his colleagues, psychiatrists Dinah Miller and Annette Hanson, coauthored *Shrink Rap*, which aims to demystify psychiatry for both lay and professional audiences. The book is based on the team's popular blog of the same name, which gets thousands of hits per day, as well as their podcast, which is online at MyThreeShrinks.com.

As director of Pitt's Biomedical Informatics Training Program, **Rebecca Crowley** (MD '94) oversees some 30 core faculty, 50 affiliated faculty from 25 University departments and centers, and 40 grad students. Plus, she adds casually, she "teaches and all that stuff, too." The associate professor of biomedical informatics, intelligent systems, and pathology has taught post-graduate classes for 10 years. Recently, she was awarded two American Recovery and Reinvestment Act supplements to support new students, faculty, and course offerings.

Crowley's research interests include using technology to develop teaching tools and information systems for research. She's working on several federally funded projects, including Cancer/Text Information Extraction Systems (a highly detailed, anonymous, patient-report system for biomedical researchers) and SlideTutor (an intelligent tutoring system that guides new pathologists through their training).

'00s

At Pittsburgh's Hilltop Community Healthcare Center, pediatrician **Amy Nevin** (Pediatric Resident '02) is making a difference for children in the economically disadvantaged neighborhoods hidden in the hills above the city's South Side, where 90 percent of her patients are on Medicaid. She educates groups about the dangerously high lead levels she sees among her patients and has even advocated to have dilapidated buildings demolished. "I'm like a country doctor in the middle of the city," she says. "Personal presence and relationships carry a lot of weight." **Barbara Ayars** (MD '86), Nevin's residency mentor at Wilkinsburg Family Health Center, greatly influenced her. "She taught me to look outside of the office to see how poverty and physical and psychiatric illness around a child affect that child's health."



Nevin

—Brian Connelly, Megan Kopke, Marc Melada, Elaine Vitone, and Alexis Wnuk



Ellis' initiative helps doctors care for cancer patients.

patient subpopulation.

Ellis says this program has been shown to slow the rise in the cost of cancer care in the region. And in a recent internal review, UPMC Cancer Centers found that the hospitalization rates in their breast cancer patients were actually reduced, though survival rates stayed the same. "Because we're not giving people a toxic regimen they shouldn't get," says Ellis.

Each center uses a common Intranet system designed especially for UPMC, which has built-in features designed to make oncologists' jobs easier, like flagging patients for genetic testing to determine whether certain drugs are safe for them. Several practices across the country have purchased the system. "We've had the compliment of people wanting to copy us," says Ellis. "Dana-Farber called and said, 'How'd you do this?' and the Mayo Clinic called and said the same thing." *—Elaine Vitone*

YOU NEVER WRITE ...

We want to hear your news: career advancements, honors you've received, volunteer work, publications, and we love to hear old Pitt memories.

To get us your news, drop us a line at medmag@pitt.edu or see our postal address on the inside front cover.

SEYMOUR M. ANTELMAN

OCT. 27, 1938–JUNE 10, 2011



Antelman

Perhaps the most enduring contribution of Seymour "Sy" Antelman is his study of dopamine systems in normal and abnormal behavior. Prior to the PhD's 1975 *Science* paper, the only known function of the neurotransmitter was movement. Antelman, a Pitt professor emeritus of psychiatry, died in June.

Using an animal model of unexpected stimulus (a pinch on the tail), Antelman found that the resulting increased dopamine-system activity heightened the animal's response to biologically important aspects of its environment (e.g., food, threat, offspring). "What changes is your outlook," says Henry Szechtman (PhD '75), professor of psychiatry and behavioral neurosciences at McMaster University in Hamilton, Ontario, who worked with Antelman as a graduate student. "You need dopamine not just to move but also for things to be interesting. Without it, you can't assess and appraise." This finding helped elucidate the relationship between mental illness and stress.

Later in his career, Antelman focused on Time Dependent Sensitization (TDS)—a model in which the effects of drugs and of stress increase as time progresses—which stirred controversy. But Antelman enjoyed a good argument, Szechtman says of his old, vertically gifted friend. "Tall trees catch more wind." —*Elaine Vitone*

B. FRANKLIN DIAMOND

JAN. 30, 1942–MAY 17, 2011



Diamond

B. Franklin Diamond (MD '67, Res '69) established the Stroke Center at Abington Memorial Hospital, the first Joint Commission-certified stroke center in Pennsylvania. He also created the Diamond Stroke Tool, a protocol to help EMTs recognize strokes in the field and deliver the best pre-hospital care. Diamond himself succumbed to a stroke in May at the age of 69.

"Frank was way ahead of his time in terms of realizing the importance of stroke centers and in terms of rapid treatment, which is so critical to the success of treating a patient with a stroke," says David Eskin, an MD, former chief of staff at Abington Memorial Hospital, and a close friend of Diamond.

Prior to joining the staff at Abington in 1974, Diamond served in the U.S. Air Force for two years as chief of neurology at Sheppard Air Force Base in Texas. From 1993 to 2007, he was Abington's chief of neurology.

Eskin frequently referred patients and family members to Diamond; he saw the neurologist as intelligent, creative, and compassionate. He was the "kind of person that I wanted to take care of a member of my family," he says.

—*Alexis Wnuk*

IRENE JAKAB

JULY 15, 1919–JUNE 18, 2011

In 1974, Irene Jakab launched Western Psychiatric Institute and Clinic's (WPIC) John Merck Program for children with intellectual disability and co-occurring psychiatric disorders. Today, Merck is part of a continuum of WPIC services for dual-diagnosis patients throughout the life span—the only program with this distinction, notes John McGonigle, assistant professor of psychiatry. An early recruit of WPIC director Thomas Detre, a fellow Hungarian, Jakab directed child psychiatry at Pitt throughout the '80s and developed a training program on dual diagnosis that was attended by physicians from around the world. As an emeritus professor, in 1989 she returned to Massachusetts—she'd held an academic position at Harvard since 1966 and was still a lecturer there at the time of her death.

Among her devoted old "Mercky" friends, Jakab is sorely missed. She supported patients' interest in art and Special Olympics. She threw grand holiday parties—think live Christmas tree adorned with lighted candles and Hungarian candy. (McGonigle stood by with the fire extinguisher.) She encouraged professional development in every level of her staff. "Susan," she asked mentee Susan Glor-Scheib in her thick accent, "you *will* go get your doctorate someday, won't you?" Glor-Scheib is now professor of special education and clinical services at Indiana University of Pennsylvania. —*EV*



Jakab

KALIPATNAPU N. RAO

MARCH 7, 1937–JULY 4, 2011



Rao

Even after retiring from Pitt's pathology department in 2004, Kalipatnapu N. Rao, a PhD, maintained his interest and work in clinical and forensic toxicology, chiefly in writing a textbook, *Forensic Toxicology: Medico-legal Case Studies*, which he finished just a few weeks before his death in July.

The longtime pathology professor and native of India came to Pitt in 1971 as a research associate. In 1989, he became chief of toxicology in the Division of Clinical Chemistry, a position he held for 15 years. He also served as the director of the laboratory group for Toxicology and Therapeutic Drug Monitoring for UPMC Presbyterian and Children's Hospital of Pittsburgh of UPMC.

Beyond his highly respected research in pancreatic carcinogenesis and the management of patients with toxins exposure, Rao will also be remembered as a great listener. He preferred to discuss clinical and scientific topics with colleagues and students over a cup of tea, says Mohamed Virji, an MD/PhD and pathology professor. Rao recognized the importance "of getting individuals away from the busy laboratory environment so that issues could be addressed objectively," he says. —*AW*

IN MEMORIAM

'40s

EDWIN BAYLEY BUCHANAN, MD '47
APRIL 23, 2011

'50s

JOHN H. WILKINSON MD '50
FEB. 2, 2011

E. DAVID CHERUP MD '51
NOV. 23, 2010

ROBERT E. SCHNEIDER, MD '54
MARCH 26, 2011

HAROLD W. SLONE MD '55
JUNE 10, 2011

MICHAEL R. ZERNICH MD '57
JUNE 1, 2011

DONALD H. QUINT MD '59
MAY 5, 2011

'60s

ROBERT J. DONOVAN MD '60
JUNE 17, 2010

CHARLES PAUL GENNAULA MD '63
NOV. 7, 2010

ROBERT GOLDWYN FEL '63
MARCH 23, 2010

SAMUEL C. MINES MD '63
APRIL 8, 2011

'70s

ROBERT JENKINS JR. MD '70
JUNE 13, 2011

'80s

DAVID SERVAN-SCHREIBER RES '87
JULY 24, 2011

FACULTY/STAFF

ARTHUR PHILLIPS JR.
APRIL 24, 2011

GEORGE F. THIERS
JUNE 9, 2011

BROCKTON HEFFLIN BRINGS NAMING RIGHTS TO THE MEDICAL ARENA

BY SHARON TREGASKIS



FRANK HARRIS

What's in a name? Hefflin builds a taxonomy for safety.

In the Biblical account of creation, Adam named the animals of the Earth in a single day. Eighteenth-century Swedish botanist Carl Linnaeus, the father of modern taxonomy, spent more than two decades cataloguing both plants and animals for his *Systema Naturae*. Medical epidemiologist Brockton Hefflin (MD '90) has spent the last 14 years creating a taxonomy of another sort—a searchable, online catalog of medical devices.

As a Washington, D.C.–based medical officer in the U.S. Food and Drug Administration, Hefflin serves as cochair of the expert team overseeing the Global Medical Device Nomenclature (GMDN) project, an international effort to create a standardized system for naming and categorizing all medical devices—from acupuncture needles to prosthetic toe joints.

"Medical devices reach the borders of all countries now," says Hefflin, noting that patient care often involves treatment with items designed and manufactured overseas. "It's important to be able to identify devices in the post-production arena. Approval [in the United States, by the FDA] takes place with a clinical trial, but we need to perform post-market surveillance after a device is approved. Having a standardized nomenclature helps to facilitate that."

Launched in the early '90s by European Union officials hoping a shared vocabulary would ease the reporting and tracking of safety data and adverse events among member countries, the GMDN has grown to contain 20,000 preferred terms (e.g., *polydioxanone suture*), each with an associated code and definition, as well as more than 1,000 collective terms (e.g., *suture* and *bioabsorbable*). Already, the database has been translated into more than 25 languages, including every official tongue of the European Union.

Perhaps the most challenging element of Hefflin's work with the GMDN has been developing the intellectual framework to accommodate thousands of existing medical devices—all regularly modified by their manufacturers—as well as those yet to be invented. "We're constantly editing the terms," says Hefflin.

He and cochair Alan Fields, a British engineer, review 30 applications for new terms every month, with help from a committee comprised of an in vitro–diagnostics expert from Australia, a radiological-device expert from the Netherlands, and a U.S.-based cardiovascular-device expert from Ghana.

Hefflin, a 48-year-old Pittsburgh native—whose travels as a volunteer medical missionary have included stints in Guatemala, Haiti, and throughout Africa—credits two mentors with putting him on the path his career has taken.

His father, Charles Hefflin (MD '74), a lifelong learner who worked as a microbiologist and then a dentist before becoming a family physician in Shadyside, urged his son to enroll at Pitt for an MD. While the elder Hefflin was a clinician "par excellence," in his son's words, the younger Hefflin—intrigued by medical anthropology and international health care—was ambivalent about clinical work; still, he took his father's advice.

After completing his MD, he enrolled in the Centers for Disease Control and Prevention's Epidemic Intelligence Service (EIS) post-graduate program.

His EIS training assignments included investigations of the health effects of the fuel additive methyl-tertiary-butyl-ether in Alaska, seasonal dust storms in Washington State, and exposure to mercury in latex exterior paint used by professional painters in California's Bay Area.

Hefflin recalls how Pitt's former dean of students Fred Rubin, an MD, pointed him toward the EIS:

"He recognized that my interest went beyond anatomy and physiology." ■

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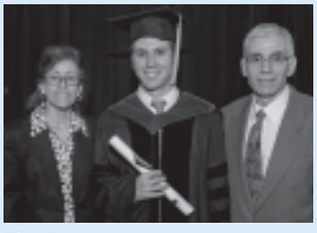




LEFT: John Donatelli holds his son on graduation day, 1985. **RIGHT:** On graduation day this May: the Donatellis.



The McNeil Bregars



The Grecos



TOP: The Class of 1936, including Paul Caplan (indicated with red arrow). **SHOWN HERE:** Paul Caplan with Josh and David Levenson.



The Lewises



The Thomases

RECENT PHOTOS: CIDDE AND THOMAS FAMILY

THE ONLY SCHOOL OF NOTE

Chris Donatelli (MD '11) was just 5 months old when his father, John Donatelli (MD '85), graduated. Photographers snapped pictures of the new doc holding his little boy, and his little boy holding his diploma. The young Donatelli remembers looking through all the books in his dad's home office, and how, even as a child, he thought about being a doctor like his dad.

A total of six of the Class of 2011's freshly minted MDs are keeping it in the family. Amy Bregar's (MD '11) parents, Melissa McNeil and Frank Bregar, graduated together in 1980. Nicholas Greco's (MD '11) dad, Frank Greco, graduated in 1978, and his mom, Maria Costa-Greco, followed two years later. Richard Lewis, father of Clayton Lewis (MD '11), graduated in 1973. Vanessa Thomas (MD '11) is a third-generation Pitt meder, with both her parents and her paternal grandfather calling Pitt their alma mater.

Josh Levenson has more than one familial connection to the School of Medicine. His father, David Levenson, is on the clinical faculty at Shadyside Hospital, and Levenson got to work with him during one of his clinical rotations. "It was a great bonding experience," he says.

Levenson's great uncle, Paul Caplan, is a member of the Class of 1936 and, at 97 years of age, our oldest living alumnus. Caplan, who recently endowed a research grant in perpetuity for the Department of Rheumatology, read the Hippocratic Oath at his great nephew's White Coat Ceremony four years ago. "You had no choice, you were going to go to the University of Pittsburgh," Caplan told Levenson. "That's the only medical school in the country of note," he said laughing. ***—Alexis Wnuk***

CALENDAR

OF SPECIAL INTEREST TO ALUMNI AND FRIENDS

For information on an event, unless otherwise noted, contact the Medical Alumni Association: 1-877-MED-ALUM, 412-648-9090, or medalum@medschool.pitt.edu. Or go to www.maa.pitt.edu

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