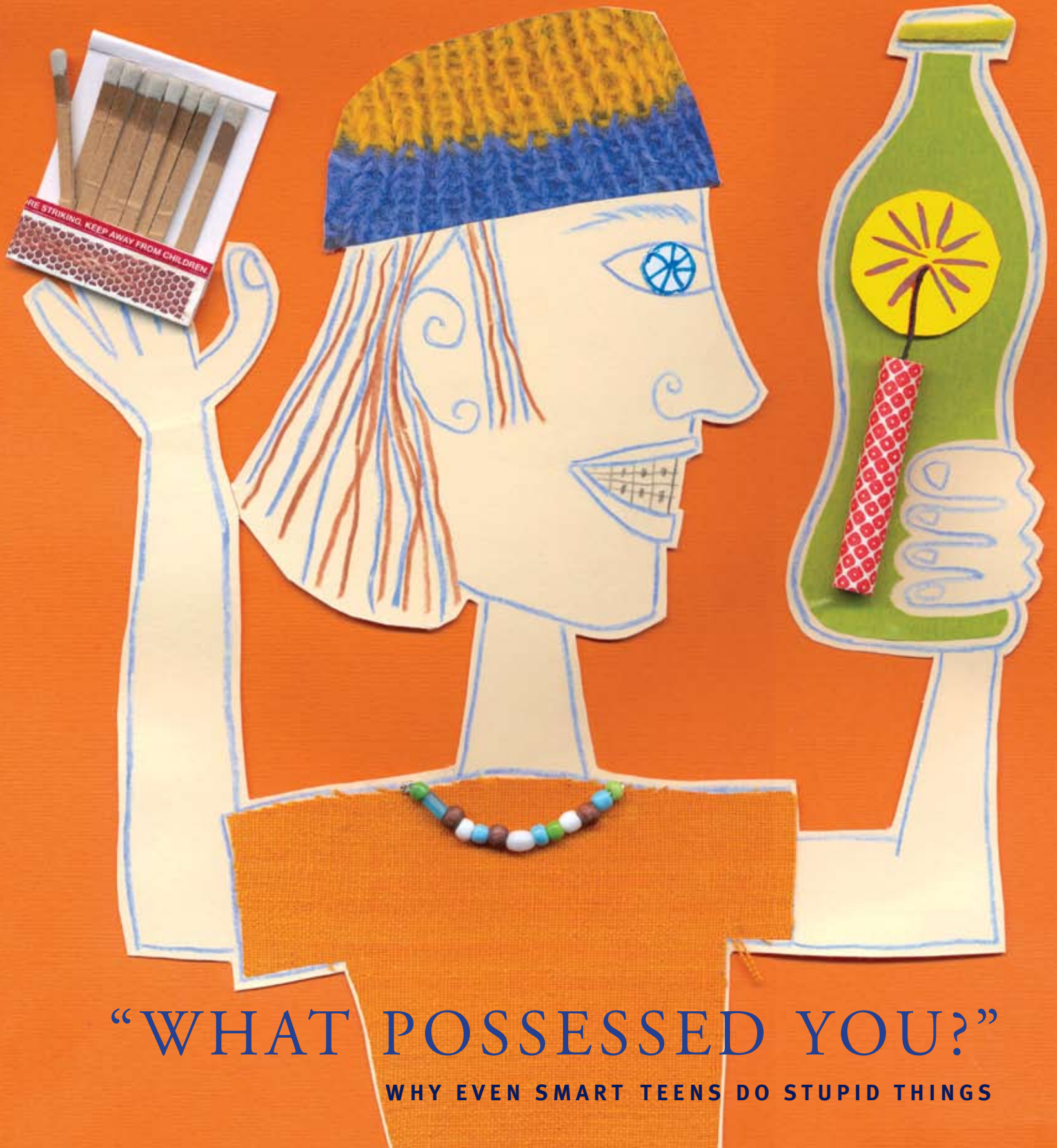


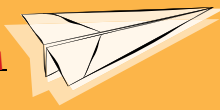
UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | FALL 2007

# PITTMED



“WHAT POSSESSED YOU?”

WHY EVEN SMART TEENS DO STUPID THINGS



## BEFORE SIMULATIONS

I am a 1965 graduate of Pitt's medical school. I have enjoyed reading *Pitt Med* over the years, but have not been back to Scaife Hall since my graduation. I was struck by Elaine Vitone's article "The Modern Deathbed" (Summer 2007). When I became a physician, we did not make use of simulations or actors to portray dying patients.

During my time at Pitt, the medical curriculum was dichotomous. The first two years were mainly classroom lectures in a variety of sciences. The last two years were purely clinical. When we walked out onto the wards to start our junior year, one was expected to have certain basic skills: how to do a history and a physical, basic lab exams, start an IV, draw blood, pass an NG tube, put in a urethral catheter, do a spinal tap, etc.

Following graduation, I was assigned as a Navy intern at Philadelphia Naval Hospital. This was during the height of the Vietnam War, and the average daily census ran close to 4,000 patients. We had a grand total of 18 interns and were on watch every other night. During this year, I had a growing respect for the education that I had received at Pitt. Some interns were simply overwhelmed by the volume and nature of the diseases that were commonplace at Philadelphia. Pitt had prepared me well. There were too many patients and too few staff to expect to have your hand held. You either had to fish or cut bait. At times, there was no other physician available to help you.

I began my residency in urology at Balboa Naval Hospital on July 1, 1968. My chief resident asked me if I knew anything about testis tumors. I told him that I had heard that they were rare. He then asked me if I knew anything about chemotherapy of testis tumors. I told him I didn't know a thing about that. He then told me that I should get up to speed as quickly as possible because we had 14 patients on the ward with metastatic testis tumors and that I was going to be their chemotherapist. There was not a department of oncology in existence at that time. All of my testis tumor patients died. I developed my own style of dealing with death and dying.

A few years later, I became the chairman of Balboa's urology residency program at the ripe age of 37. I tried to teach by example. I also tried to help my residents come to grips with death and dying. I later performed the same job at the University of California, San Diego School of Medicine, before retiring in 1994.

Despite the lack of actors or simulations in my training, I attribute most of my success to the medical education I obtained at Pitt. I was fortunate enough to take a senior elective in psychiatry. I learned to pay critical attention to the verbal and nonverbal communications of patients while on that service. That experience, along with the basic sciences and excellent clinical experience provided by Pitt, contributed greatly to my success as a surgeon and teacher of surgeons.

I always look forward to reading *Pitt Med* and wish Dean Arthur S. Levine continued success as the leader of one of this country's finest medical schools.

Michael P. McCarthy (MD '65)  
Carlsbad, Calif.

*To read the full text of Dr. McCarthy's letter, including his memory of being the medical officer for a squadron of Navy submarines when one, the USS Scorpion, was lost at sea, go to:*  
[http://pittmed.health.pitt.edu/Fall\\_2007/letter/](http://pittmed.health.pitt.edu/Fall_2007/letter/)

## DISTINGUISHED COMPANY

My belief that the Pitt Med Class of '62 is special was confirmed by "Defining Moments" (Summer 2007). Braverman, Brenner, Hibbs, and Kushner are certainly deserving of acclaim. However, you failed to mention other members of the class who achieved fame in clinical fields.

George Leopold was called the "Father of Clinical Ultrasound" and chaired the radiology department at the University of California, San Diego. Chuck Kerber was a pioneer interventional neuroradiologist at the University of Oregon. Tom Provost performed major research in dermatology at Johns Hopkins. Jim Theodore excelled in pulmonary medicine at Stanford until his death in 2003.

The combined achievements of this elite group would certainly qualify Pitt Med '62 as a candidate for all-time, all-star status!

Don Kaiserman (MD '62)  
Santa Monica, Calif.

## KUDOS

Your article "Plain People, Complex Cures" was stunning (Summer 2007). I took a particular interest because I am from Lebanon, Pa., a mere stone's throw from the horses and buggies of which you wrote. I have shared the story with my family. Thank you for the fascinating read.

Katy Rank Lev  
Pittsburgh

Your article on Alexis Chidi was remarkable ("Pre Pitt Med," Summer 2007). You captured her vibrant spirit, inquisitiveness, intellectual fearlessness, lack of self-absorption, and her wit, and also highlighted the "graduate guarantees" programs, specifically the BS/MD program at Pitt med!

The article gives the reader a clear idea of what kind of physicians and scientists Pitt med is investing in and grooming. It provides concrete proof of senior vice chancellor Art Levine's statements in earlier issues about Pitt placing high value on physicians who have maintained a visceral interconnectedness to their communities even as students and who have not shied away from being agents of positive change. I view it as

a continuum, which includes the Pitt med students who work as concession stand and catering employees to raise money for an AIDS clinic and those who volunteer countless hours to staff a free clinic, in spite of their rigorous schedules.

I have enjoyed reading many of your past issues and articles, including "Make Like a Salamander" (Fall 2006). As producer and host of *Page 2 Pantry* on Pacifica Radio KPFK 90.7 FM Los Angeles and 98.7 FM Santa Barbara—which deals with a broad range of health, nutrition, and policy issues—I naturally enjoy news of interesting, cutting-edge research which holds great promise for health and wellness. I find *Pitt Med* magazine first-rate in content, style, and production value.

On a final note, I love your catchy titles and bylines. Keep up the great work!!

Niki Guluchi  
Lawndale, Calif.

We gladly receive letters (which we may edit for length, style, and clarity).

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# PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE, FALL 2007 (AUG/SEPT/OCT)  
VOL. 9, ISSUE 3



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## CONTRIBUTORS

Illustrator **CATHERINE LAZURE** [Cover, "What Possessed You?"] hunts New York City streets for her materials: a fruit box outside a local bodega, bottle caps on the ground, used books, sushi containers, a plastic snake duct-taped to a tree. She finds items and brings them to her Manhattan apartment, where her boyfriend stares at her and says, "Where did you get that?" Lazure invites the challenge these random items bring to her work. "My closets are completely full with junk," she says, "but I welcome playing with chance and accidents. I found a lot of cross-pollination when I started bringing things home. My aesthetic influenced my projects, and my projects influenced my aesthetic."

Tired of the newspaper grind, writer **JOE MIKSCH** ["Crime Scenes"] left Connecticut and returned to Pittsburgh in 2005. He submitted his résumé for scores of "real jobs" and began narrating Just Ducky tours—conducted in an amphibious World War II era "duck boat"—to feed himself, plus his wife, cat, and dog. When *Pitt Med's* senior editor, Chuck Staresinic, informed Miksch that the staff was interested in his application, Miksch was surprised: "I don't even remember applying for the job," he says, joking. "I thought I applied to *Pitt Magazine*." He's been *Pitt Med's* associate editor since July 2005 and is especially gleeful that he never again has to cover a municipal government meeting.

## COVER

Pitt neuroscientists are discovering reasons why teenagers engage in risky behavior.  
(Cover: Catherine Lazure ©2007.)



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## PITTMED

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**M**y fortieth year had come  
and gone and I still throwing  
the javelin.

—Samuel Beckett,  
“Horn Came Always”

Playfulness in science is a notion that engages me. In recruiting students and faculty, I seek creativity, which seems to me to be encoded by a different gene than the one for intelligence—and an unlinked gene at that. As Steven Connor of the London Consortium has written, play is about creativity, an aesthetic idea, and about winning and losing, an athletic idea.

Creativity means making something out of nothing, or at least very little (imagination), and it is reflected in our perceiving similarities among disparate things. Great scientists make these connections freely, welcoming that intellectual tension, and they have a great capacity for metaphor and intuitive discovery. Looked at this way, it would seem profitable for granting agencies to spend as much time thinking about the *person* of the applicant as about his or her proposal. The history of the person who had the idea should be as interesting as the history of the idea.

A profile of Robert Lang in *The New Yorker* this past February captures this idea. Lang is a physicist and an origami master—perhaps this country's leading practitioner of that old art. He was given an origami book at age 6 by a teacher who could no longer keep Lang interested in arithmetic but who appreciated that paper folding involved principles of math as well as of art. From that time through his Caltech graduate studies and to the present, Lang has folded ever more complex structures, now involving hundreds of steps—making something out of nothing. His structures inform not only basic science (molecules such as proteins must fold and unfold in predictable and compact ways), but also applications such as a mesh heart support that is implanted in a patient with heart failure via a very thin catheter; when released from the catheter, it unfurls properly and elegantly around the heart. Origami appeals to Lang, and many others, for its simplicity and seemingly endless possibilities.

Now about the second element of play—games and sports, winning and losing. This involves individual competition. (And who would deny that research is hypercompetitive, especially now?) There is competition in the existential sense of illuminating or failing to illuminate nature. Winning or losing as a team, which characterizes much of contemporary biomedical research, is serious business. Even so, by the very definition of play, we are not *obliged* to do this. It is fun, as science should be. We know, however, that children who have no opportunity to play often have cognitive dysfunction, and that animals that are especially “playful” (e.g., ravens and Norway rats, as noted by Konrad Lorenz) have the greatest likelihood of survival in new habitats.

We seek these two elements of play—aesthetic and athletic—in our students because, confident in their ability to “think outside the box,” they will make fine diagnosticians. We seek these qualities in our researchers because making something out of nothing is a risk-taking strategy involving winning and losing, and that's what great science is about. The greatest risk-takers in research are often the young, not constrained by dogma. It is that cohort in particular that we must protect in a time of granting-agency conservatism.



JULIA MAROUS STRAUT

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



*Devoted to noteworthy happenings at the medical school ... To stay abreast of school news day by day, see [www.health.pitt.edu](http://www.health.pitt.edu).*

## Royal Treatment

Angus Thomson was recently elected to the Royal Society of Edinburgh, Scotland's national academy of science and letters. The Scotsman is a professor of surgery, of immunology, and of molecular genetics and biochemistry at the University of Pittsburgh School of Medicine, as well as director of transplant immunology and associate director for basic research at the Pitt-UPMC Thomas E. Starzl Transplantation Institute.

Thomson is internationally known for his contributions to understanding the role dendritic cells play in transplantation tolerance and immunity. —Joe Miksch



CAM MESA

Angus Thomson

## FOOTNOTE

When David Hollander, creator of the CBS series *The Guardian*, was growing up in Pittsburgh, he followed the news about surgeon Thomas Starzl. To research *Heartland*, his new TNT television drama about a transplant team, he came home. Experts from the Thomas E. Starzl Transplantation Institute helped him plot the inner workings of the fictional Pittsburgh-based St. Jude Regional Transplant Center.

## PITT EXPECTS TO STAY STRONG WHILE RESEARCH DOLLARS IN U.S. STAGNATE

In his May State of the School address, Arthur S. Levine, senior vice chancellor for the health sciences and dean of the University of Pittsburgh School of Medicine, noted that National Institutes of Health dollars support 75 to 80 percent of the academic biomedical research in the United States.

Then he pointed out that while applications for NIH grants have doubled since 2003, the purchasing power of the \$27 billion NIH budget has decreased 13 percent because budget allocations haven't kept up with inflation. Levine and other medical school top administrators are pushing Congress to boost the NIH budget by 6.7 percent a year for three years. Making that happen, Levine said, will take some time, yet it is only enough to get back to 2003 funding levels. He also offered more immediate remedies, such as pursuing support from the state, as well as from industry and private foundations.

Levine says the school is well positioned to thrive in the face of limited funding. "By recruiting researchers who are likely to net NIH grants, by retaining senior faculty with longstanding NIH funding, and by investing in infrastructure and emerging areas of inquiry," he says, "the School of Medicine should get its share of a limited pool of dollars." —JM





A&Q

## On Their Honor

Before prospective students are admitted to the School of Medicine—at the interview, in fact—they each receive a copy of the *Student Code of Professionalism*. The 13-page honor code is written by Pitt medical students.

Students elect nine representatives (two from each class plus one MD/PhD student) to serve on an honor council to “effectively model and communicate” the code. The council serves as a resource for students trying to resolve issues and, in rare instances, participates in disciplinary procedures.

Pitt’s council was created in 1998, partly through the efforts of two inspired alumni of Pennsylvania’s Haverford College, where the honor code is a central part of undergraduate life. A current member of the honor council, Bryan Ward (Class of ’09 and shown above), is another Haverford graduate. Cynthia Lance-Jones (also shown above), a PhD associate professor of neurobiology, is one of three faculty members nominated by the students to serve on the honor council.

### Why the code matters

**WARD:** The honor code, in spirit, is a manifestation of what life is going to be like as a physician—having everyone, in a way, looking out for each other. [Medicine] is very much a community, and there’s a cooperative feeling.

### The role of the council

**LANCE-JONES:** The honor council is there to help solve problems before they become huge and to have the students learn to solve problems. The faculty’s role is to help them learn to confront their peers in a good, constructive, valuable way.

Most young people are not very comfortable confronting a peer to say, “That’s not good. You signed that chart without looking at it.” Or, “You signed into a class when you weren’t there the whole time.” As future doctors who will work in groups and must trust in professional behavior, they will have to do this before [a problem] gets really big.

### The honor code’s evolution

**WARD:** After first year, I took a trip back to Haverford and scoured through the school library’s archives and found a book about the honor code’s history. One of the big steps forward in the history of Haverford’s honor code was creating a plenary, a forum where students could discuss the honor code and participate in its evolution by writing amendments, rewording clauses, etc. Having students participate was a way not only to generate visibility, but also to validate that it was something the community believed in. [The medical school’s first plenary was held in January 2006.]

### Their question for us

How might students who are not on the honor council take greater ownership of the honor code?

—Interviews by Chuck Staresinic

## Faculty Snapshots

**A**ngela Gronenborn, the UPMC Rosalind Franklin Professor and chair of the Department of Structural Biology at the University of Pittsburgh, has been elected to the National Academy of Sciences. Membership in the academy, founded in 1863, is one of the highest honors a scientist can receive. Gronenborn, a PhD, is a leader in nuclear magnetic resonance spectroscopy, a tool used to define the structure of proteins and other vital biomolecules. The discipline of structural biology has become a key part of the drug discovery process.

**Jeannette South-Paul (MD ’79),** reared in Philadelphia, saw crippling poverty firsthand as a child because her parents ran a rescue mission in the city. Today, as the Andrew W. Mathieson Professor and chair of Pitt’s Department of Family Medicine, she hasn’t strayed far from her caring roots.

South-Paul recently received the American Medical Association’s Pride in the Profession award in recognition of her altruistic approach to practicing medicine. In addition to her administrative role, South-Paul has sponsored a holistic wellness program at an underserved Pittsburgh high school and sees patients at the Matilda H. Theiss Health Center, a clinic that offers care to community members, including the indigent and uninsured.

“I like to focus on making a difference in the lives of people who have no voice,” she says. “My piece is to try to model community service and a commitment to caring in everyone we train.”

**The American Society for Clinical Investigation has added Pitt’s Yuri Nikiforov to its rolls.** The ASCI honors physician-scientists with significant, early-career achievement in scholarly biomedical research.

Nikiforov, an MD/PhD professor of pathology who directs both the Division of Molecular Anatomic Pathology and the Molecular Anatomic Pathology Lab in the School of Medicine, studies the mechanisms of radiation-induced carcinogenesis. He works to develop molecular tests to diagnose thyroid cancer.

**The Association of American Physicians’ roster now includes Pitt’s Augustine Choi and Louis Faló.** Choi, an MD professor of medicine and chief of the Division of Pulmonary, Allergy, and Critical Care Medicine, has shown that low doses of carbon monoxide, coupled with oxygen therapy, inhibit oxygen-induced damage to lung cells. Choi is in a small vanguard of scientists studying the beneficial roles of carbon monoxide in the body.

Faló, an MD/PhD, is a professor of dermatology and chairs the department. His work has implications for vaccines against HIV, melanoma, lymphoma, and diverse infectious diseases. —JM



Gronenborn



South-Paul



Nikiforov



Choi



Faló

## Reading is Fundamental

The text is an excerpted transcript of a physician talking with a patient who suffers from back pain. But what's the subtext? Robin Maier asks her students to sort it out. Maier, an MD and volunteer clinical assistant professor of family medicine at the University of Pittsburgh, wants her students to apply the tools of Marxian, feminist, structuralist, or deconstructionist literary theory.

The mini-elective Medicine and Literature, Maier says, is intended to help students communicate more effectively with patients by encouraging them to think more precisely about the implications of the words they say and hear in the clinic.

Zachary Zator, a first-year med student, chooses the Marxian perspective. Maier asks him, "Well, where's the money here?"

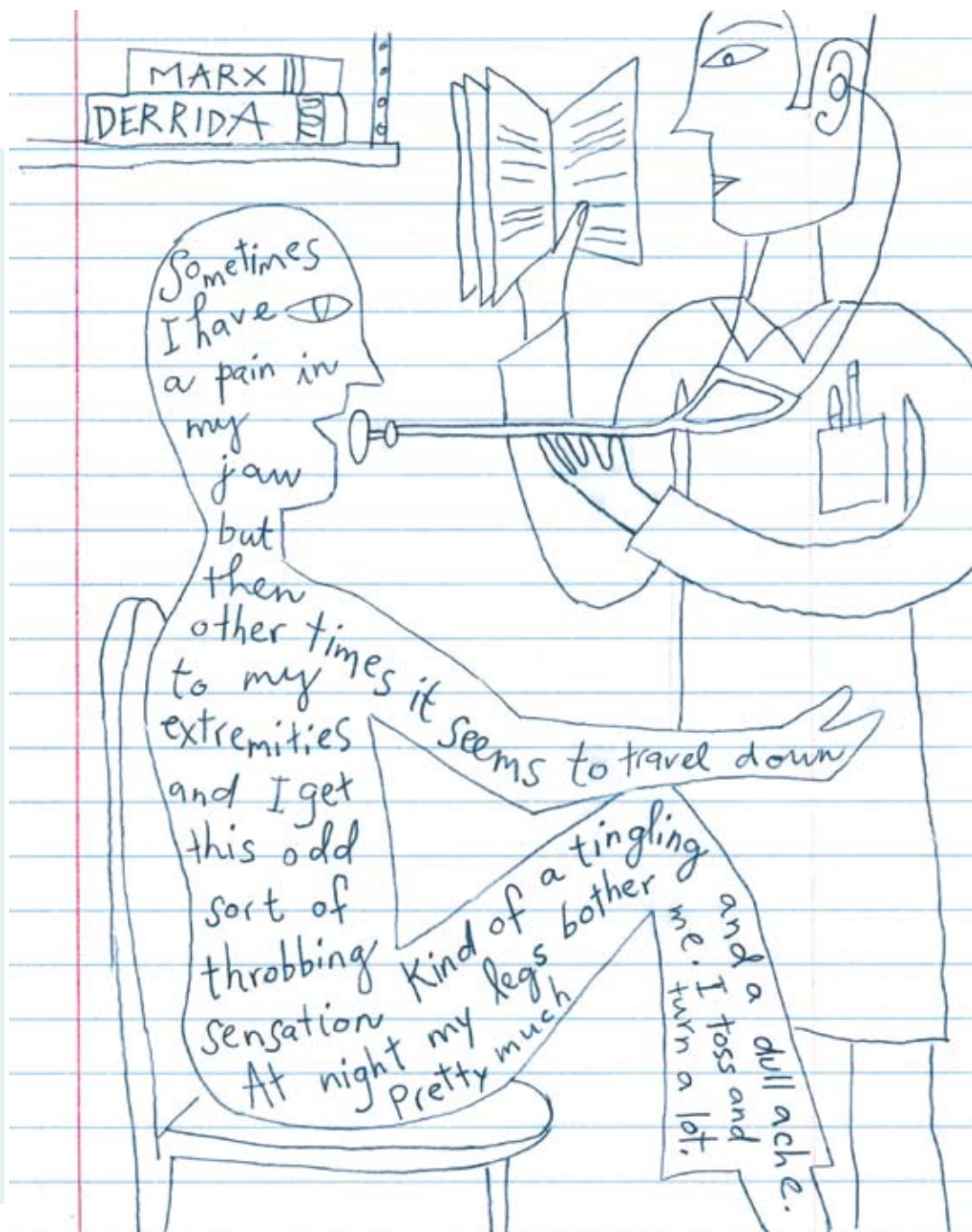
"In the prescriptions they're talking about," he responds.

"How about bed rest?" she asks. "Is that expensive?"

"No," says the student.

"It can be if you have a job you can't afford to miss," Maier points out.

The conversation extends into a discussion of Medicaid, welfare reform, and the relationship between money and medicine. All from a few lines in a transcribed doctor-patient interview. —JM



CATHERINE LAZURE

## NIH DOUBLES SUPPORT FOR PHYSICIAN-SCIENTISTS

It takes about \$500,000 to mold an MD/PhD over the course of the University of Pittsburgh/Carnegie Mellon University Medical Scientist Training Program (MSTP). Of the 100 on this path to becoming a physician-scientist, nine slots are fully funded by the National Institutes of Health.

Make that 18. The NIH recently announced that its funding of the Pitt/CMU MSTP will double by 2009. From July 1, 2007, through June 31, 2010, the program will receive a total of about \$3.7 million in NIH funding above the 2006 level.

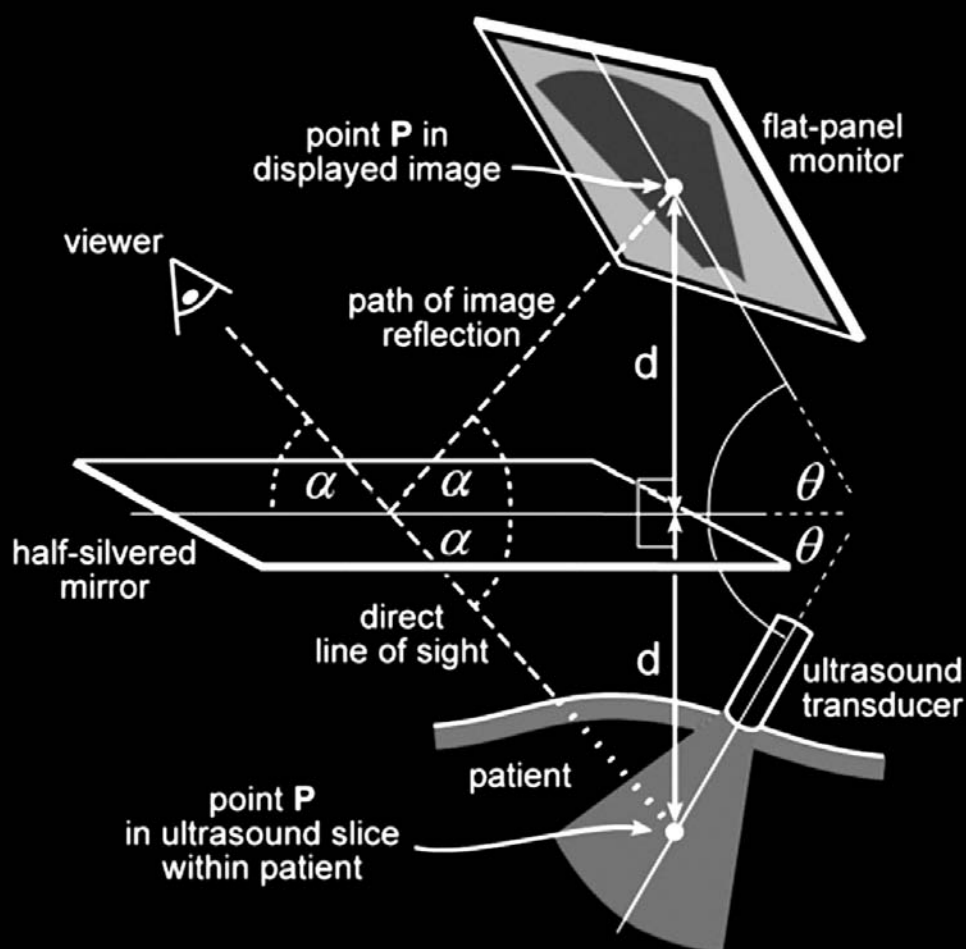
"It's an impressive number," says Clayton Wiley, associate dean for the MSTP and an MD/PhD professor of pathology. "It's difficult to get new slots because they are so very costly and very competitive."

Wiley says that when the time came in June 2006

to apply for renewal of NIH funding, the MSTP chose to seek the increase. They were not optimistic. "To get a new position [another school] has to lose a position," Wiley says, adding that the NIH funds a finite number of slots. "Someone had to lose, and given the current NIH funding environment [see "Pitt Expects to Stay Strong ..." on p. 3], there were questions as to whether that would happen."

Wiley says he considers the funding hike a testament to the quality of the MSTP. He also sees it as a way to further increase the number and quality of applicants to the program, which trains biomedical researchers with an eye toward interdisciplinary investigation and creative collaboration. "It's nice to see the program getting recognized, and it's nice that we will be able to continue to bring high-quality individuals to Pittsburgh." —JM





## SONIC FLASHLIGHT

It's kind of like those x-ray specs advertised in the back of old comic books, except this little device can actually see through flesh and has real medical uses.

The device, called the sonic flashlight, was invented by George Stetten, an MD/PhD associate professor of bioengineering at the University of Pittsburgh. The handheld ultrasound tool allows users to keep their attention on the patient, rather than on a separate ultrasound screen.

Doctors are experimenting with using the device to help them insert catheters into patients' veins. Nikhil Amesur, an MD associate professor of radiology, is conducting the clinical trial. (To see how the optics work, check the image on the left.) —JM

## Name Dropping

The 2007 Senior Vice Chancellor's Laureate Lecture Series at the University of Pittsburgh began in May with a visit from **Peter Schultz**, a PhD and Scripps Professor of Chemistry at the Scripps Research Institute in La Jolla, Calif.

Schultz, a member of the National Academy of Sciences and the Institute of Medicine, has made vital contributions to understanding the interface of chemistry and biology. He discovered methods to generate catalytic antibodies and developed biosynthetic ways to insert unnatural amino acids into proteins. The latter feat may permit scientists to create a new generation of proteins that can work as novel catalysts and drugs.

Schultz has served on the faculty of the University of California, Berkeley, was a Howard Hughes Medical Institute Investigator, and is the director of the Genomics Institute of the Novartis Research Foundation.

As part of the Laureate series, Nobel Laureate **Linda Buck** will present, on September 27, the lecture, "Unraveling the Sense of Smell." Her talk will dissect the underlying molecular mechanisms of the olfactory system, including the ability of the nose and its workings to detect and differentiate at least 10,000 distinct odors and translate them into what, in the brain, are perceived and recalled as specific smells.

Buck, a PhD, is also interested in exploring how smells affect reproductive physiology and behavior. She is a member and associate director of the basic sciences division at the Fred Hutchinson Cancer Research Center in Seattle.

During her visit, Buck will receive the 2007 Albert C. Muse Prize for Excellence in Otolaryngology from the Eye and Ear Institute and Eye and Ear Foundation.

**Sherwin Nuland** spent his medical career at Yale University, starting with med school. He eventually rose to the rank of clinical professor of surgery and fellow of that university's Institution for Social and Policy Studies.

Nuland's 1995 book, *How We Die*, was on the *New York Times* best-seller list for 34 weeks, won the National Book Award, and was a finalist for the 1995 Pulitzer Prize and the Book Critics Circle Award. He has nine other books to his credit.

The physician-author addressed the University of Pittsburgh School of Medicine Class of '07 at its May commencement. He says the aim of his speech was to remind the newly minted physicians of the humanistic aspect of their careers.

"We must restore our pastoral role at the bedside and sustain the human spirit of all who come to us for healing," he says. —JM





## FAST TALKING

Geoffrey Bond may be the fastest surgeon around.

Somewhere in Nebraska this spring, Bond and a passenger were doing about 80 in a 65 mph zone. Law enforcement was not pleased; an officer pulled them over. "He was a nice guy and gave us a warning," says Bond. "We took pictures with him. Then, about three miles down the road, he was coming after me again, and this time I knew I wasn't speeding."

Turns out the cop wanted copies of the photos. In addition, the officer pledged to give Bond a few bucks—an unusual end to a traffic stop. Why?

Bond was driving as fast as he could to help transplant patients. And no, this wasn't a scheme for offering his own organs to be harvested.

The assistant professor of surgery at the University of Pittsburgh School of Medicine and transplant surgeon at the Thomas E. Starzl Transplantation Institute gassed up his Lotus Exige S and spent a week in May tearing about various oval tracks, drag strips, and road courses to raise money to support transplant patients who can't afford immunosuppressant drugs and to raise awareness of the need for transplantable organs. (Bond recommends speeding on official courses, only, rather than public highways. Yet he admits that when the patrolman stopped him, he was rushing toward the next race. After Bond explained why he was in the mood to move fast, the officer declared he would solicit his colleagues to donate to the cause.)

The 2007 Tire Rack Cannonball One Lap of America race began and ended in South Bend, Ind., spanning 18 events in seven days and covering nearly 4,000 miles, ranging from Salt Lake City, Utah, in the West, to Lexington, Ohio, in the East. Bond's Lotus was festooned with the names of sponsors who covered his costs and donated to the Odenbach Fund of the Starzl Institute. A poster promoting organ donation came along for the ride.

Bond finished 31 in a field of nearly 100—19 places ahead of his 2006 finish.

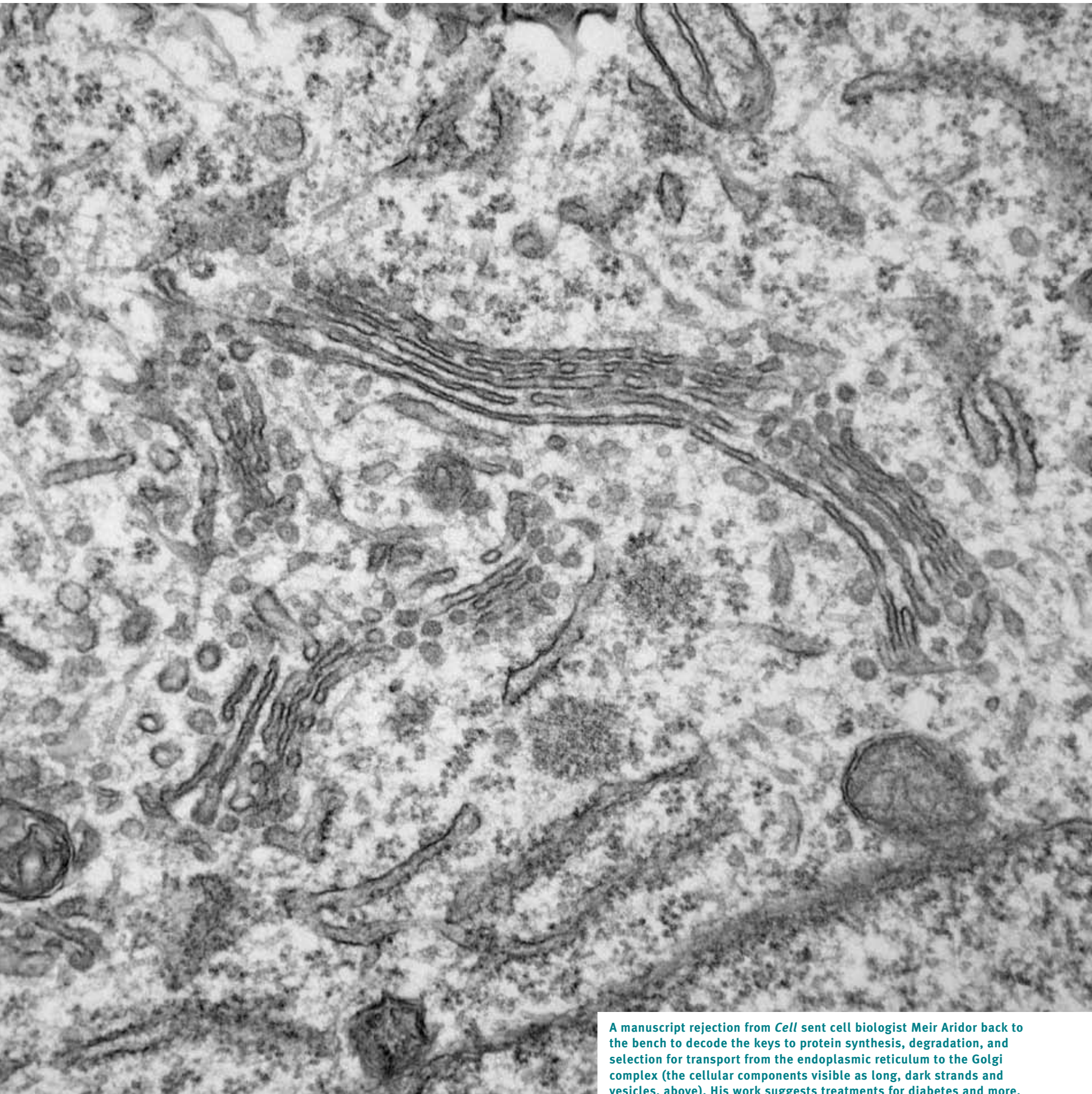
—Joe Miksch

—Photo by Steve Rossini



## INVESTIGATIONS

*Explorations and revelations taking place in the medical school*



A manuscript rejection from *Cell* sent cell biologist Meir Aridor back to the bench to decode the keys to protein synthesis, degradation, and selection for transport from the endoplasmic reticulum to the Golgi complex (the cellular components visible as long, dark strands and vesicles, above). His work suggests treatments for diabetes and more.



# SPECIAL DELIVERY

THE CELL'S SORTING MACHINE COULD BE KEY  
TO FUTURE THERAPIES | BY JOE MIKSCH

A cell is under a microscope. An organelle is seen sending out tiny vesicles, little budding bubbles. What's in them? What controls the packaging and, really, what is this thing—the endoplasmic reticulum, known as the “ER” to cell biologists—doing?

Meir Aridor has made real progress toward answering these questions and, in so doing, has made his mark on cell biology. His work helped change the prevailing view of the ER from an indiscriminate processor of proteins to a highly selective mechanism.

And this selective mechanism, he expects, will be key to developing more targeted therapies for a wide range of diseases.

Aridor is a PhD assistant professor of cell biology and physiology at the University of Pittsburgh. Prior to the early 1990s, he says, the ER—where the cell synthesizes, processes, assembles, sorts, and degrades proteins—was poorly understood. Investigators knew the “what” of the ER, but had little idea regarding the “how.”

Scientists saw the ER as a passive mechanism, explains Aridor, one that allowed newly synthesized proteins to diffuse through the system.

“The assumption was that everything was free to diffuse ... that the ER and the secretory pathway worked like a distillation tower,” he says.

That view began to change when Aridor and others noted that small vesicles budding from the ER contained specifically selected proteins. Further study showed that a coat protein complex, called COPII, resided on the vesicles' surface.

“In 1994, COPII was defined as a coat that can make vesicles in yeast,” says Aridor. “We were the first, though, to show that it did the same thing in mammalian cells.”

Aridor and colleagues demonstrated that COPII was responsible for protein movement out of the ER.

There was a small problem, though.

“We sent the paper to *Cell*, and it was a year in review,” Aridor says. “The upshot is that they

came back to us and said, ‘This is interesting, but we don't believe it.’”

The problem, he concedes, is that the paper was based upon the analysis of visible phenomena, without explanation of the mechanisms involved. “I realized we had to determine the molecular basis of the process [to gain credibility]. Until we understood the interactions, we couldn't actually have these claims.”

The rejection from *Cell* spurred years of lab work that pinned down the mechanisms and molecules responsible for selecting the protein cargo tucked into vesicles leaving the ER. Among the components Aridor and his lab mates characterized was a protein called Sar1 that is responsible for deforming the ER membrane to detach vesicles. It's also been Aridor's quest to unearth molecules responsible for cargo selection and for sending the protein-laden vesicles to particular destinations.

On a recent sunny and hot Pittsburgh afternoon, Aridor sat behind his desk and talked about the cell's protein packaging and sorting mechanism, which has been the focal point of his career since the early 1990s.

Describing his investigations into the ER's functioning, Aridor often seems on the verge of levitating above his chair. His hands wave, his bushy, graying hair sways, and his voice rises to punctuate the thrill of discovery.

Aridor's colleague Ora Weisz is a PhD associate professor of medicine in the renal electrolyte division. She has authored two papers with Aridor and describes him as “a big thinker. He has a really amazing ability to think big thoughts on a microscopic level. He's trying to unravel how, in the most basic way, proteins that are newly synthesized get out of the earliest step in the secretory pathway.”

Recent work, on which Weisz collaborated, aimed to sort out the role lipids—functioning as signaling molecules—play in the ER. “Just in the past few weeks, we've identified proteins that bind the coat and specific lipids,” Aridor

says. “And we have preliminary data to suggest that this is how the ER exit site is organized.”

Weisz says understanding the interaction between lipids and the COPII coat proteins is another step toward solving the mysteries of the ER. “Meir is beginning to develop a very mechanistic picture of how the cargo comes to one side, how the lipids remodel in order to change the curvature [of the membrane], and how the coat is recruited during this process to enable formation of vesicles,” she says.

On a practical level, Aridor sees understanding the ER as a means to understanding a slew of diseases. He is in the process of updating a list of maladies—seven pages long in 2002—connected to malfunctions in intracellular transport: diabetes, Alzheimer's disease, and myeloma, to name just a few.

Understanding the ER will offer opportunities for new therapies in the near future, says Aridor. Take high cholesterol. Drugs now in use, such as statins, inhibit enzymes that participate in cholesterol synthesis.

“They also effectively disable export of viral proteins out of the ER,” Aridor adds. This entirely blocks the synthesis of cholesterol, which is needed by cells. In an experimental system, cells die. In people, however, enough cholesterol is introduced through diet so the potential ill effects of the drug are limited.

One day, Aridor says, we may be able to control the traffic from the ER and thus the activation of just one transcription factor that regulates cholesterol level. This more specific targeting, made possible by understanding the individual components of the ER, would eliminate such possible adverse effects and allow for more effective drugs.

“The nice thing about this is you can study basic physical interactions and the insights, and you can learn a lot of stuff in terms of function and diseases,” the scientist says. “I'm a little bit excited about this. Look at the possibilities.” ■



The monotone voices of children with autism helped orient Nancy Minshew's studies.

# AUTISM: A CASE OF MIXED SIGNALS?

PITTSBURGH RESEARCHERS FIND EVIDENCE  
FOR THEORY | BY REID R. FRAZIER



Every day, the children from the inpatient ward at Pitt's Western Psychiatric Institute and Clinic would whoop it up on their way to gym. Every day, Nancy Minshew could hear the voices in the hallway outside her office, even through her closed door.

"I could tell which children had autism based on their voices. They were often loud, and they spoke with a monotone."

This was during the mid-1980s, when Minshew had first come to the University of Pittsburgh as a pediatric neurologist. A colleague at the University of Texas had recently shown how stroke hindered prosody—the melody of a person's speech. Children with autism lack prosody. Minshew now says hearing those monotone voices helped orient her toward studying how autism works in the brain. Children with autism could do the essentials—like speak—but struggled with more complex aspects, such as modulating their speech.

a metaphor or play "make believe." Kids with autism don't do "make believe" very well.

"I had one kid tell me, 'Don't you understand? I don't play with things that aren't real,'" Minshew says.

She has long subscribed to a theory of disordered complex information processing and underdeveloped neural systems. That is, that autism affects the brain's connections, not just one of its regions. For a study Minshew coauthored last year, she gave 56 children with autism a series of neuropsychological tests, then compared their performance with that of their nonautistic peers. The results: Children with autism perform well on basic functional tests but fail on complicated ones. They could find Waldo in a "Where's Waldo?" picture. But they couldn't identify different people with similar faces. Minshew says this suggests that the brain's individual areas work fine, but they don't work together to perform complex operations.

Minshew also helped turn Bernie Devlin's attention to autism. Devlin, a statistical geneticist (think big computers and incredibly long lines of genetic code), had been working on the genetics of schizophrenia and eating disorders. Minshew urged him to attend a conference in Italy a few years ago on the genetics of autism. (Since autism tends to run in families, many scientists believe it to be genetic.) A plant geneticist by training, Devlin devoured a stack of papers on the subject during the 12-hour trans-Atlantic flight. He got hooked. The allure of the problem was its complexity—there is probably no single gene for autism, but many that together convey risk.

Devlin later joined the Autism Genome Project, an international team of more than 150 geneticists trying to crack the disorder's genetic code. The group studied DNA samples from more than 1,000 people with autism in their families and found a series of genes that tend to correspond with autism.

## Kids with autism have no trouble with the basics of mental function—they can see, hear, and remember facts. The problems come when many parts of the brain have to cooperate.

Autism remains a mystery to doctors and scientists of all stripes; yet Minshew, with other Pittsburgh researchers, is starting to make sense of it.

The disease impairs social interaction and communication. Children with autism often can't remember faces. They can't read facial expressions. They have few friends. They can become inconsolable if they experience a change in routine—a detour on the way to school, a substitute teacher, or the appearance of the moon during the day.

When Minshew started studying autism, most psychologists were looking for a single culprit—one region of the brain that caused the disease. Minshew thought the problem had to be in many parts of the brain. Kids with autism have no problem with the basics of mental function—they can see, hear, and remember facts. Many have normal IQs. The problems come when several parts of the brain have to work together, like when trying to understand

Carnegie Mellon neuroscientist Marcel Just, one of Minshew's collaborators, used functional magnetic resonance imaging to watch the brains of 17 adults with autism and 17 without as they read and answered questions. In the brains of people with autism, the signals weren't as well synchronized among frontal regions and the other brain areas as they were in the control group. The results were the most convincing to date on underconnectivity, Minshew says.

Minshew directs Pitt's Center for Excellence in Autism Research, one of six such National Institutes of Health-funded centers in the country. She and her collaborators are seeking the biological and genetic causes of autism and, ultimately, new diagnosis and treatment methods. Beatriz Luna, one of the center's coinvestigators, is studying the brains of adolescents with autism to determine when intervention can be effective. (For more on Luna's studies, see article on p. 19.)

Of the body's 30,000 genes, some get duplicated or deleted ("knocked out," in geneticist parlance) when passed from parent to child. The scientists are looking at whether a series of genes related to the transmission of the chemical glutamate gets copied or knocked out in patients with autism. Glutamate is an important neurotransmitter that plays a role in memory and learning. A problem with glutamate transmission could be significant to understanding how the brain's signals become blurred in autism.

"We're sifting through a massive amount of data to figure out what's real and what's not," says Devlin, who is the group's lead computational geneticist. "We'll know a lot in about two years. But I predict we'll never know everything about it." ■

FOR MORE INFORMATION OR TO JOIN A STUDY:  
1-866-647-3436  
[www.pittautismresearch.org](http://www.pittautismresearch.org)





AS THEY TACKLE DAUNTING DISEASES,  
THREE STUDENTS LEARN ABOUT MORE  
THAN MEDICINE | BY REID R. FRAZIER

# BREAKING GROUND

About once a week over the past year, Kate Dickman hopped in a 4 x 4 with a team of nurses and social workers, colleagues on a tuberculosis research project. They would bump along Kampala's rutted, muddy streets *en route* to the Komamboga Health Center. If Dickman ever wanted a reminder of why she was in Uganda, she had only to look out the window. They'd roll past billboards advertising free HIV testing and condoms. Dickman would see young mothers begging, men sleeping in piles of garbage.

Although Uganda is one of the more stable countries in sub-Saharan Africa, AIDS has exacted a toll on the economy, adding to the poverty visible out the window of the 4 x 4.

The vehicle often stopped in Kawempe, a dense neighborhood of brick, mud, and stucco homes slumping into one another under corrugated tin roofs.

For three med students, a year abroad revealed the ties among history, culture, economics, and disease. Susan Wong worked in the former capital of China, Nanjing (left). In Uganda (below and center), Kate Dickman confronted the ravages of HIV and tuberculosis. In Zambia, Krista Pfaendler assisted in surgery (below, right).

PHOTOGRAPHY | COURTESY K. DICKMAN, K. PFAENDLER, AND S. WONG



"It's extremely crowded," Dickman says. "There are people everywhere, motorcycles everywhere, cars everywhere."

The area also has one of the highest rates of TB in the city. The neighborhood's cramped houses, often shared by several families, are fertile breeding grounds for disease. TB is transmitted by a rod-shaped bacterium called *Mycobacterium tuberculosis*, usually passed through the air when a carrier sneezes or coughs. While Dickman waited with the driver, the Komamboga clinic "home visitors" would give TB tests in the neighborhood. Sometimes they'd take people with them to the clinic.

By the time they got to Komamboga, she says, another 100 people—mothers with infants, the elderly—would be waiting in line.

As one of three University of Pittsburgh med students accepted into the Fogarty International Clinical Research Scholar Program, Dickman (Class of '09) had taken a year off from Pitt to join clinicians and clinical researchers striving to stamp out TB in Uganda.

Those who know her describe Dickman as soft-spoken and humble. In her spare time, she trains for marathons.

"She loves studying, and she loves to run," says her father, Jim Dickman. She is also driven to make a difference. "She chose to study one of the top three killers—that was not a fluke," says Catherine McEllistrem, a molecular epidemiologist and Pitt assistant professor of medicine on staff at the VA Pittsburgh Health Care System who mentored Dickman.

"From the get-go she has focused on 'How can I help reduce some of these globally devastating diseases?'"

Dickman grew up in Fort Jennings, Ohio, a no-stoplight hamlet in the state's northwest corner. Her parents still talk of how she filled their basement with Petri dishes for a junior high science fair project. After her first year at Pitt, she worked in western Kenya on a malaria research project run by Pitt's Douglas Perkins, assistant professor of infectious diseases and microbiology in the Graduate School of Public Health. There she saw children die from treatable diseases. Before she even got home, she e-mailed her Pitt med classmates about starting a charity for HIV-infected children. (The students' Kenyan Pediatric HIV Project has raised more than \$20,000 to date.)

Yet no other experience has stretched Dickman like her year in Uganda. Working with researchers at the Uganda–Case Western Reserve University Research Collaborative, she saw firsthand how medical science runs

squarely into a welter of social, cultural, political, and economic realities. How else could TB—a treatable, curable disease—kill 26,000 people a year in Uganda and more than 1.6 million annually around the world? Dickman knew the role that poverty plays. She knew that in sub-Saharan Africa, economics and politics could strangle medicine. She knew that doctors struggle to get the resources they need and that many patients lack access to health care. After a year in Uganda, she views the problems in a different light.

"I had known a lot of these things were true before I came here," she says, "but once you're here, you really see just how many things go into impacting a person's health."

Tuberculosis dates to antiquity. Egyptian mummies show signs of the disease, and the African societies living in what would become Uganda were probably already familiar with it when the British colonized East Africa in the late 1800s. Europe's TB epidemic, which had raged since the 1600s, had peaked by then, but another was going strong in North America.

In the 20th century, improved public health and antibiotics would help contain TB in

sleuthing—looking at whom treatment fails and why. Through DNA fingerprinting, Dickman studied whether some patients whose treatments failed carried more than one strain of *M. tuberculosis*. She suspects that drugs for one strain can "miss" another strain a person is carrying, as a study in China found.

Throughout, she's learned from watching Ugandan doctors like Luzze treat patients with a fraction of the resources available in the United States. "Because they don't have a lot of resources to order tests on their patients, they think really hard about which ones are absolutely necessary," she says. "In the U.S., you often just order them all without thinking too much about what it's going to tell you."

Despite the dedication of local doctors, the roadblocks to progress in fighting TB in Uganda can seem immovable. Few labs there can even take TB cultures. Some of Dickman's samples have lived for the past decade in refrigerators that occasionally heat up during power outages. The year has tested her emotional bandwidth, Dickman admits.

"You sit down and see patients, and you feel like you've helped," she says. "Then you find out

## The neighborhood's cramped houses, often shared by four or five families, are fertile breeding grounds for TB.

North America. But it thrived in Africa amid the rapid urbanization and industrialization of the colonial era; deteriorating social and economic conditions exacerbated the epidemic.

TB has rebounded everywhere in the wake of HIV and AIDS, especially in poorer countries. Of those who contract TB today, 95 percent live in the developing world. Most of the 2 billion people worldwide carrying *M. tuberculosis* will never get sick from it. But when HIV suppresses immunity, an otherwise resistant TB carrier succumbs more easily.

"HIV and TB make each other worse," says Henry Luzze, research director of the Uganda–Case Western collaborative. AIDS has helped make tuberculosis the second-biggest killer in the world.

Luzze's team is investigating how HIV and TB interact. The group is interested in the role tumor necrosis factor-alpha (TNFα), a protein produced by both HIV and TB, plays in advancing HIV. They are studying whether antiretroviral drugs can inhibit its production and slow the onset of AIDS.

The group is also doing some bacterial

later your cultures are contaminated and open up a paper and see that some bus crashed up in the countryside, and 16 people were killed. A lot of my days I feel on top of the world. And the next minute, I'll feel like all I want to do is go home and go to bed."

The research offers solace—Dickman believes her findings can help save lives down the road. This fall she'll be back in Kampala, continuing her research on a fellowship from the Howard Hughes Medical Institute. "There are certain things now that people shouldn't be suffering from. The thing is, you feel you can really make a difference with these diseases, because the problem seems so basic."

Medical students often travel to other countries to work for short spurts on healthcare projects—Dickman did so in Kenya. The idea is to expose students to other cultures and health disparities in the developing world. Along the way, these excursions point some toward a career path in global health. For others, they deepen understanding of culture's influence, probably making



them better doctors in the long run. For all of the benefits, students often use up more resources—in time and attention from the host institution—than they can contribute during their short stays.

“A student has enormous needs,” says Gerald Keusch, former director of the National Institutes of Health’s Fogarty International Center, which aims to improve health care in the developing world. (He’s now Boston University’s associate provost for global health and associate dean for global health in the university’s School of Public Health.)

“They’ve got to be taken care of. They need to find housing. They need to learn how to get around. Any bit of attention taken from patient care is a diversion from the underlying need.”

So Keusch and his Fogarty center colleagues decided to design a global health program that would reap more rewards in host countries. The time commitment—a year between third and fourth year—would attract only the most dedicated medical students. “No tourists,” is how Keusch puts it. The program also trains one medical student from each host country.

The Fogarty scholars spend a year on a mentored clinical research project in the developing world, helping to refine training, procedures, and treatments for use in areas known by experts as “resource-poor settings.”

Host institutions need to find out what works best, says Aron Primack, the program’s director (whose son is Pitt assistant professor of medicine Brian Primack, Res ’02).

“If you buy drugs, throw them on the dock, and say ‘So long,’ you haven’t really accomplished much,” he says. A big budget and good intentions go only so far.

“We need knowledge,” says John Mellors, professor of medicine and chief of infectious diseases at Pitt. Mellors worked with Dickman and Krista Pfaendler (Class of ’09), another Pitt med Fogarty scholar, on the Kenyan Pediatric HIV Project, which the two started along with their classmate Kasia Mastalerz (Class of ’09).

A retrovirologist who has worked on AIDS in Africa, Mellors says clinical research helps make the most out of any money spent in global health.

“We can’t just roll out programs we don’t know are effective,” he says.

Dickman, Pfaendler, and Susan Wong (Class of ’09) are the University’s first Fogarty scholars. (There were 23 from the United States.) Dickman and Pfaendler applied their Fogarty studies toward their scholarly research projects. This fall, Pitt med student Yetunde Olutunmbi



(Class of ’09) will travel to Tanzania as the fourth Pitt Fogarty scholar. There, the Nigerian-born, U.S.-raised Olutunmbi will study the link between maternal nutrition and fetal AIDS transmission.

Beyond their clinical research training, the scholars also learn problem-solving—how to deal with shortage, delay, and other common frustrations that hinder health care in poorer countries. Thuy Bui, the medical director of Pitt’s Program for Health Care to Underserved Populations and assistant professor of medicine, says such skills are vital when working in resource-poor areas in the United States, too.

“You have to use your clinical acumen and make decisions the old-fashioned way,” says Bui, who returns every summer to the hospital in Malawi where she worked as a Peace Corps volunteer doctor in the 1990s. Many of Bui’s students fret about the medical problems they’ll encounter in the developing world.

“They worry they don’t know enough about the science of malaria. I say, ‘You’ll be fine with that. The harder question is, What do you do when you have no more staff at the clinic? What will you do then?’ They don’t believe me until they get there.”

The first woman off the bench one day last fall at the Kanyama Clinic was in her 60s or 70s. She wore a skirt and headwrap made of chitenge, the colorful traditional cloth of Zambia. She was thin but did not look particularly sick.

Krista Pfaendler pulled on latex gloves and seated the patient on the exam table inside a tiny white room. Pfaendler had been in

**From Zambia, Pfaendler (second from left) went to Tanzania to see former Fogarty scholar Anna Acosta and local healthcare providers.**

Zambia a month and knew only a few words of Nyanja, the local tongue. (Zambia has 72 languages.) She had learned how to examine the cervix, watching the clinic’s nurse-midwife use forceps to apply cotton soaked in acetic acid (essentially vinegar), wait a few minutes, then check the color of the cervix. White tissue was a red flag for cancerous or precancerous tissue and meant a referral for more tests. The procedure, called visual inspection with acetic acid (VIA), is used in Zambia instead of the relatively costly Pap smear.

The day before, Pfaendler had sent all the clinic’s patients home after the nurse called in sick. When the nurse called in sick a second day in a row, Pfaendler kept the patients in the clinic while she made a call.

“I didn’t feel right sending them back,” Pfaendler says.

She phoned her supervisor, Mulindi Mwanahamuntu, a gynecologist who oversees a national cervical cancer screening program. He told her she could conduct the screenings with a peer educator in the room as a translator. If she had any problems, she could fetch one of the other medical officers in the clinic.

Pfaendler started the procedure.

“I knew what it was when I saw it and smelled it,” she says. The smell was necrosis, dead tissue caused by invasive cervical cancer. She’d only seen cases this advanced in textbooks. In all probability, the cancer had already spread.

On her third-year rotations at Pitt the year

before, Pfaendler had been alone with patients, making treatment decisions, but always with the approval of a nearby resident or attending physician. This was different.

"She was sick, and I was the only one there who could do anything about it. It was kind of frightening," she says. She told the woman she needed to see a doctor immediately because she most likely had cervical cancer. Pfaendler knew the woman would likely get palliative care, at best. A biopsy later confirmed Pfaendler's suspicion—the patient had inoperable cancer.

A week later, the woman approached Pfaendler on her way into the clinic. The woman seemed like a weight had been lifted from her. That surprised Pfaendler a little.

"She was all smiles and thanked me profusely for sending her to [the hospital]," Pfaendler says. "I think she was just appreciative to have someone listen to her and to give her an answer as to what was going on, even though I told her there was nothing we could do for her."

Pfaendler grew up in a multilingual household in York, Pa. Her father is a German-speaking native of Switzerland; her American mother teaches French. She wasn't put off by the dissection of a bull's eye in school, unlike so many other kids, says her mother,

ried speculums back and forth from clinic to hospital to autoclave them for re-use. When the electricity quits, the clinicians still perform exams, using flashlights and natural lighting.

Parham, a University of Alabama at Birmingham gynecological oncologist with more than 20 years of experience in Africa, found an astonishing 94 percent of HIV-positive Zambian women tested had abnormal Pap smears. As with TB, HIV lowers the body's natural defenses against the human papillomavirus, which causes cervical cancer. Consequently, cervical cancer is the leading cause of cancer-related death in sub-Saharan Africa, the killer of 270,000 women a year worldwide. Now that many HIV-positive women are taking antiretroviral drugs, they will live long enough to contract cervical cancer. With access to early detection and care, they will survive it. The clinicians can remove worrisome tissues through simple, quick procedures like cryotherapy, which destroys problem cells through freezing, or surgery using a small, looped, electrical filament. In Zambia, where the HIV rate is between 12 and 16 percent—and as high as 25 percent in Lusaka, where the clinic is located—the need for better screening and treatment is obvious.

But how to do it on a shoestring?

listening. CCPIZ has screened more than 7,000 patients so far.

While readying a room one morning this February for that day's surgical procedures, Pfaendler found they were nearly out of lidocaine, a local anesthetic. A visiting doctor from Ukraine suggested they tell the 20 or so women lined up in a stairwell awaiting treatment to come back the following week. Pfaendler demurred. She knew many of them had traveled far and might not return. Even a 25-cent bus fare could deter those whose households earn less than a dollar a day.

Pfaendler couldn't reach her supervisor. The hospital staff complained about the women in the stairwell (the clinic had no bench). The doctor again suggested they send the women home. Pfaendler still resisted. She had already learned that when women came to the clinic, you never knew if you were going to see them again. Soon, the staff found the lidocaine. They operated that day on the patients.

**S**usan Wong was in Beijing four years ago studying Chinese during the initial stages of the severe acute respiratory syndrome scare. When news arrived that SARS had reached the city, she watched pandemonium descend. Her music teacher left in the middle

## **"I think I came in with typical American bravado. I'm realizing I still have a lot to learn."**

Sue Pfaendler. She spent a month in Ecuador one summer during college with Child Family Health International, rotating through various clinics. The experience showed Pfaendler a potential career path, one that combined medicine with immersion in a different culture.

This past year, Pfaendler has learned the ins and outs of clinical research—including writing grants, getting consent, and building protocols. And as Thuy Bui predicted, she's learned how to make things happen.

Groesbeck Parham, who runs the Cervical Cancer Prevention Institute of Zambia (CCPIZ), says there are two eras in the short life of his three-year-old program: "pre-Krista" and "post-Krista." When she arrived last summer as a Fogarty scholar, Pfaendler was charged with organizing the center's screening program. She received a crash course in what Parham calls "the entropic law of doom." The clinic runs out of latex gloves; speculums get hung up in customs; the electricity goes out. For each hurdle, Pfaendler has learned to craft a solution. She and colleagues have fer-

Zambia is one of the poorest countries in the world, with a per-capita gross domestic product of \$1,000. Because they don't have the money or the staff to run expensive diagnostic equipment, Parham and codirector Mwanahamuntu are refining homegrown techniques for the nine screening centers they have set up. Pfaendler spent much of her year studying one such method, digital cervicography, whose main component is a common digital camera. The camera—fitted with a macro lens—is wired to a television to image the cervix. Pfaendler says the method "greatly improves" diagnosis with VIA. And when women see their cervical lesions on the screen, they're more likely to return for treatment.

For inspiration, Pfaendler can point to two Zambian docs, Mwanahamuntu and Graciella Mkumba, a consultant on the project. They have preached cervical cancer prevention on radio, on television, and at public events.

"They both have passion for this problem, and it rubs off on those around them," Pfaendler says. It appears Zambian women are

of a class. "People had no information," she says. "The public was left completely in the dark, reaching for anything."

The experience made Wong think about how the public receives its health information. When she arrived at Pitt the next year, she volunteered at the health clinic of the Women's Center & Shelter of Greater Pittsburgh, and later became a health literacy worker. As a second-year med student, she started a medical literacy program for Somali refugees in Pittsburgh, along with fellow student Olutunmbi.

This past year, Wong has been a Fogarty scholar in Nanjing, at China's National Center for STD and Leprosy Control. After a 25-year absence, syphilis has returned with a vengeance in China, and many worry that HIV might not be far behind. Researchers elsewhere have found that genital ulcers—like those caused by syphilis—might facilitate HIV transmission. With her Chinese colleagues, Wong is studying whether there is a "dual epidemic" of HIV and other sexually transmitted diseases. She says she's become particularly interested in the





**ABOVE: A year in Nanjing gave Wong (not pictured) a chance to forge new connections with her extended family. RIGHT: Friends from work helped Wong (second from left) navigate the local culture as she studied STDs.**



feminization of STDs in China.

The rise of syphilis there is tied to a perfect storm of biology, economics, politics, and social factors. With the discovery of penicillin in 1939, syphilis, which is caused by the spiral-shaped bacterium *Treponema pallidum*, became easily treatable. Syphilis was prevalent in China until Mao Zedong came to power in 1949. Mao's sweeping public health campaigns were effective, if brutal. (He sentenced sex workers to "re-education camps.") In the ensuing years, China's population had virtually no exposure to *T. pallidum* and became vulnerable to it. The disease re-emerged in the 1990s with the introduction of capitalism and a growing sex trade.

The rate of syphilis cases per 100,000 people skyrocketed from 0.17 to 6.5 between 1993 and 1999. Congenital syphilis, passed from mothers to infants, has increased 72 percent a year since the early '90s.

Wong is seeing how taboo can contribute to epidemics.

While analyzing test results for a large STD survey in China this year, she noticed that some patients reported they'd never engaged in risky behavior, yet their serology tests showed that they, or people they had slept with, had.

Doctors, too, sometimes skirt topics like homosexuality, drug use, and prostitution. Wong heard one doctor tell an STD patient, "Don't go out too much. Cut down on drinking and smoking," to avoid future infection.

At the same time, she's seen Chinese doctors and scientists on her team determined to eradicate syphilis. They've created a large-scale surveillance system on the fly and provided inexpensive, patient-friendly diagnostic testing, even in the poorest corners of the country. They've also pressured the Ministry of Health

to take syphilis seriously. "I was impressed that, despite the disarray and adversity I often felt in the country, major public health initiatives were still being tirelessly fought for."

Her father emigrated from a town near Nanjing in his teens. Yet Wong had a hard time navigating China's complex social order.

"I think I came in with typical American bravado. I'm realizing I still have a lot to learn," she says. Being Chinese-American, Wong says, "I thought I would understand how things worked there. There's a way you're supposed to interact with your colleagues, and I just didn't know how it worked."

Still, she's drawn to the place. "When you see something happening to people who share your heritage, it just hurts," she says. She feels less like an observer now; she is thinking more about how to contribute to solving some of the public health challenges the country faces. Being sensitive to the cultural context has been critical in that evolution, she says.

She'll be back in China this August. On a Dean's Fellowship from the medical school, she'll mine data from the country's largest hotline to study the relationship between domestic violence (specifically, intimate partner violence) and suicide. Unlike in the United States, most suicide victims in China are female. Wong wants to know why so many women there choose suicide.

Those who know Wong have been impressed with her sensitivity.

Lynn Hawker, former director of counseling services at the Women's Center & Shelter in Pittsburgh, said when she first heard that a med student wanted to research eating disorders among residents, her hackles went up. Hawker had seen plenty of experts come

to the shelter "who want to diagnose these women with a problem." Not so with Wong. "She wanted to look at [eating disorders] from the point of view of the women, not just from a clinical point of view. She was looking at how eating became part of the abuse. When the women talked to her, they had a real sense that she cared," Hawker says.

Wong's parents worry about their daughter's generous spirit. As an undergrad at Brown University, Wong devoted time—even during finals—to helping Southeast Asian refugees she had befriended in Providence, R.I.

"I said, 'Why are you so busy doing all these things for other people?'" Kai Ling Wong says. "She'd say, 'Don't worry, Mommy, I can handle it.'"

When Wong broke the news that she'd be taking time off from med school to spend a year (and counting) in China, Kai Ling Wong was concerned: "We said, 'Why don't you finish medical school and become a specialist?'"

Perhaps later. In the meantime, Wong is considering returning to China as an MD to promote health education or work in epidemiology. She thinks of her year in Nanjing as the first step in a long-term relationship. It is as if she were pulled back by magnetic forces.

She draws confidence from her friends in Nanjing—Chinese grad students and young physicians—who have helped her navigate "China life." They've discussed problems with their families and work. The relationships marked an important shift for Wong.

"It meant a lot that they felt they could trust me," Wong says. "I was afraid that I would always be considered an outsider to them. It made me believe that I had broken ground in China." ■







BEATRIZ LUNA IS FINDING OUT WHY  
EVEN SMART KIDS DO STUPID THINGS  
BY ELAINE VITONE

# “WHAT POSSESSED YOU?”

**R**iding down a hill in a shopping cart. Racking up a \$600 cell-phone bill. Cannonballing from a rooftop into a swimming pool. Totaling a car. Licking a flagpole in February. Lighting a firecracker in a bottle.

In those infamous years between ages 12 and 20, most kids pull a few stunts that they're not particularly proud of in the long run—things they just sort of find themselves doing that are... well, dumb. It's a real strain on parents. Besides being stuck with the thankless role of disciplinarians, a lot of parents' frustration stems from the way such episodes often seem to come out of nowhere. One day Johnny is behaving like the good, bright teenager he is, keeping up in school and doing well all around as he continues to grow taller, sharper, and more adultlike.

ILLUSTRATION | CATHERINE LAZURE

Then, the next day, *bam!* A blatant act of outright idiocy.

Beatriz Luna, Pitt associate professor of psychiatry and psychology and director of the Laboratory for Neurocognitive Development at Pitt's Western Psychiatric Institute and Clinic of UPMC (WPIC), says that the problem with adolescents may not be that they're prone to lapses of immaturity; it may be that every moment of every day, they're living in the big fat middle of immaturity, working harder at grown-up behavior than we will ever know.

"Adolescents kind of look like adults, but

and depression, emerge in adolescence. In recent months she has given talks on these and other conditions in the Netherlands, England, Germany, and her native Chile. Lately, it seems, the teenage brain is all the rage. "It used to be just me and maybe three other people presenting about it," she says. "Now [at conferences] there are 10, 20 presentations a day for all three days. It's great."

At a White House ceremony last year, Luna was one of 12 National Institutes of Health-funded researchers honored with Presidential Early Career Awards for Scientists and Engineers, the U.S. government's highest honor for those professionals getting their independent careers off the ground. Long before the award, her work had already caught the attention of a broader audience outside the scientific community because it addresses an age-old question: Why do kids do stupid things?

Broadly speaking, human behaviors can be broken down into two types—the more instinctive variety, known as reactive response (lashing out when you feel angry, for example), and the more calculated behavior that requires inhibiting the reactive response and overriding it with a consciously formulated plan (stopping yourself from lashing out and going somewhere to cool off). The latter process requires executive function or cognitive control.

The ability to inhibit responses and behave more deliberately is obviously an acquired skill. Using imaging technologies and behavioral studies, Luna is tracking the gradual shifts in the brain's structure and function to illuminate how we develop this ability that separates the men from the boys, the women from the girls.

*Discover*, *Science*, and *Scientific American Mind*. She has received letters from inmates serving life sentences: *Dear Dr. Luna, I committed a crime when I was very young. ... Can you help me?*

Reporters ask her the same questions: *Can you look at a brain and tell if someone is a violent criminal or not? How old is old enough to be accountable for your own actions? What does all this mean?*

Sometimes, it's a little uncomfortable. "I don't want to stretch what we're finding," Luna says. "But I think I have a responsibility as a scientist to try to help make sense of all this."

When she responds, her eyes narrow, the furrows of her forehead rising to form a question mark in the middle as she nods. There aren't any easy answers. It's best to start small and go from there. "Our approach has always been to take these little steps."

**J**ust before puberty, the brain has a growth spurt of its own—a disarray of new connections among parts of the brain. In order to become more efficient, the brain prunes away the connections that prove less useful. The wiring that the adolescent does end up using becomes reinforced with a white matter known as myelin—a fatty, insulative coating that protects and streamlines connections. It's a classic case of use-it-or-lose-it.

Until this process is complete, the routes that aren't fully myelinated will be slower. With too many extra forks in the roads, the adolescent brain often picks a less-than-ideal connection. Faced with this disadvantage, it's vulnerable to making mistakes.

Based on animal and cellular studies, neurobiologists have suspected as much for a while.



Beatriz Luna may actually understand teenagers.

then they do really stupid things sometimes, and you're like, 'How can you do something so stupid?'" she says, speaking from experience. Luna has a 16-year-old son and a 14-year-old daughter. "But actually, those stupid things may have a real neurological basis."

By age 10, the brain looks much like an

**One day Johnny is behaving like the good, bright teenager he is, as he grows taller, sharper, and more adultlike all the time. Then, the next day, *bam!* A blatant act of outright idiocy.**

adult's in terms of weight and size. But while the parts are pretty much all there, the wiring among them is a work in progress. These changes in circuitry are a main focus for Luna, a leader in the emerging field of developmental neuroscience—the intersection of brain-structure development and the changing behavior of adolescents.

Luna is working to establish a template for healthy brain development in teenagers. Such a template could have far-reaching implications since many disorders, including schizophrenia

She says that as the brain reorganizes its circuitry throughout adolescence, it's vulnerable to making bad calls—which might explain why a kid would insist that, somehow, setting off fireworks in the gymnasium really did seem like a good idea at the time.

Luna has given advice to inform policy on teenage pregnancy, age limits for such activities as driving and drinking, and sentencing for minors who commit crimes. She has been published widely in academic journals and interviewed by *The New York Times Magazine*,

The Luna lab has shown the effect of these developmental processes on response inhibition and cognitive control more directly and in greater depth than anyone else. The lab has demonstrated that when an adolescent completes a given task at an adult's performance level, she uses different brain systems, which are less efficient than those used by an adult.

"Sometimes the adolescent [brain] looks like a brain that's working really hard—like an adult brain doing something a lot more difficult," says Luna. "And just like an adult doing





something very difficult, [the young brain] is vulnerable to error.”

Much of Luna’s research has focused on the prefrontal cortex—that package of gray matter directly behind the forehead that plays a vital part in cognitive control. The prefrontal cortex is well connected to the rest of the brain. In adulthood, it essentially uses these connections to delegate. By sharing the workload, the brain is able to complete tasks more efficiently.

The prefrontal cortex (the slowest region to mature) doesn’t complete its growth until a person reaches her 20s. In the meantime, as

it streamlines and fine-tunes connections, it attempts to tackle complex cognitive behaviors in-house instead of delegating.

That means it often takes on more than it can handle.

And that’s why a 17-year-old talking on a cell phone in stop-and-go traffic is more likely to have an accident than a 30-year-old. For the teenager, the instinctive reaction—to freeze—is much harder to override with a cognitive response, like slamming on the brakes.

This work could have important implications for mental health research, because

every single neuropsychiatric disorder has a link to the prefrontal cortex.

“It makes sense if you think about it,” says Luna.

“All of them have in common the inability to have control over what’s coming in and what’s coming out. With schizophrenia, it’s hallucinations. With mood disorders, it’s emotions.”

A year ago, subjects between the ages of 8 and 28 made the first of five annual trips to Luna’s lab to complete what she describes as “very simple” tests as part of a longitudinal

study funded by the National Institute of Mental Health.

The tests do look simple. Sitting in a dark room with a camera focused on the pupil of one eye to record its movement, the participants face a computer monitor and perform a series of tasks involving pulses of light flashing on the screen. The monitor gives them instructions: Look directly at the flash of light. Look away from it. Stare straight ahead and ignore the light as it moves around to various points.

For those study participants who don't have hindrances like braces or claustrophobia, an encore performance follows at the Brain Imaging Research Center, a facility on the South Side run jointly by Pitt and Carnegie Mellon University. Using the center's 3 Tesla scanner, the team watches which brain networks are activated.

Although other researchers investigating cognitive control have opted for video, verbal, or pencil-and-paper tasks to study decision-making, Luna's team has chosen ocular-motor tests for several reasons. For one, eye movement is a basic, well-understood function that's been thoroughly documented in animal studies. For another, the entire brain is wired to react to a flash of light by looking at it, and choosing to override that reaction is a perfect example of the executive process. This "simple" task is useful in revealing the complex circuitry of the developing brain.

Luna's team has shown that performance on these ocular-motor tests does not improve with practice, but it does with age. For example, a 12-year-old returning to the lab every day for a week won't be able to raise his score. He will score higher the following year, however, because by then the connections in his brain will be that much closer to those of an adult.

"It's very interesting, because for 8-year-olds, when you ask them not to look at that light, 50 percent of the time they're going to look at it anyway—they can't help it," says Luna. "They look immediately, say, 'Oh no, I'm sorry,' and then they look the other way, which means: 'I understand what you asked me to do. I just couldn't stop myself.'" It isn't until puberty that they're able to perform this task as well as adults—but even then, they can't do so consistently.

Near the end of the testing, a facilitator asks the subject to perform the more difficult of the tasks again, this time with a new variable: cash.

"We want to know what reward does to the brain of an adolescent, and how does it differ from an adult's," says Luna. In adolescents, Luna's preliminary results are showing immaturities and less activation in the parts of the brain that assess the meaning and value of rewards (namely the orbitofrontal cortex). But that doesn't make kids get any less wide-eyed when the dollar signs appear on the screen. She sees this excitement in the scans, too. "The part of the brain [the ventral striatum] that gets excited about a reward is like, *Whoa!*"

She has applied for further funding to look into how kids process rewards, which she expects will lend insight into addiction and the adolescent brain.

**O**n a sunny Tuesday in early May, as Luna sits in her corner office overlooking Forbes Avenue, she talks to yet another reporter about her work. Assistant professor of pediatrics and psychiatry Miya Asato knocks at the door. "We've got some really cool brain pictures we want to show you," she says, peeking in.

"Yay!" Luna says with her characteristic almost-teenagerly zeal. (It seems that interacting with kids so much through her studies may have rubbed off on this scientist.)

Minutes later, Luna sits at a computer in an office at the opposite end of the hall, getting her first glimpses of a complex neuroimaging project more than a year in the making. Asato stands beside her, clipboard in hand, taking notes on which images they'll use in a poster they're putting together for that weekend's Cognitive Neuroscience Society conference in New York. Sitting behind Luna is Jae Kyun Woo (Class of '08), a spiky-haired electrical-engineer-turned-med-student who first put his programming expertise and interest in pediatrics to work for this project about a year ago. Woo has been coding, crunching data, and toiling away at this interface for months while MIT physics grad student Robert Terwilliger has done much of the analysis.

On the screen are three interactive images of a brain viewed from different vantage points. It's actually not the brain of any one individual, but what's known as a mean map—a sort of structural average of multiple individuals. This mean map represents more than 100 study participants. Children, adolescents, and adults are equally represented.

In each image, the gray matter is outlined (go figure) in gray; within it, a network of green lines branches throughout the brain like

limbs on a tree, marking the brain's myelinated connections. A few small red, yellow, and white sections along the branches fascinate the practically giddy Luna as she zooms in and out and moves through the brain with her mouse. These "hot spots" mark areas where the brain's myelinated connections change with age, growing with time.

"Don't you love that one, Miya?" says Luna, zooming in on a hot spot near the inferior frontal gyrus, a part of the brain that influences response inhibition and executive control. "I love it so much I think I'm gonna marry it!" says Luna.

At the conference, Woo and Asato will present their poster showing the hot spots from these images, cross-referenced with results from the ocular-motor studies. The comparison reveals several interesting results. For one, the more robust the myelinated pathways, the better subjects are able to stop themselves from looking directly at the flash of light. Specific regions of the brain associated with response inhibition were more activated in these cases as well.

Watching Luna interacting with the young researchers on her team is a bit like watching your favorite high school teacher—the one who was always popular with students for her energy, humility, and dedication to sharing her passion for the subject at hand. She's a bit of a rascal, which endears her, too. In brief breaks between brain-scan swooning sessions, she turns around and taps the vertical hairs at the top of Woo's crown, instant messages a joke to the graduate student down the hall, laughs and lets her genuine joy in her work show. In the lab she keeps a light, fun atmosphere. Off-hours, she goes bowling with her team.

"She has a lot of energy and is really passionate about her work," Woo says later. "It's hard not to get infected by that."

"She's a great mentor who's really fostered the careers of young investigators," says Asato, who's in the second year of a study on epilepsy and its effects on development and behavior.

As a child neurologist with six years of clinical experience, Asato is especially attuned to what a better understanding of the brain's circuitry could mean for patients with neurological disorders. "In epilepsy and a lot of other conditions I'm interested in, the MRI scans are normal," she says. "But we know from what the child and the family are experiencing—the seizures, the developmen-



tal problems—that the brain isn't healthy.”

Under Luna's guidance, Asato won a National Institutes of Health career development award, which funds the project. “Bea helped me prepare and learn about the research tools I needed to make that transition and become an investigator,” she says. “This has been a big thing for me.”

In the February 2007 issue of *Biological Psychiatry*, Luna published results from a study on autism, which is known to impair cognitive control. She has shown that just like people who don't have autism, those who do show dramatic improvement in cognitive control from childhood to adolescence, both in behavior and brain function. Previously, behavioral therapy for children with autism focused on the first three years of life because it is a well-recognized window of plasticity—of opportunity. This second window could be very good news for patients with autism and their families.

Ron Dahl, the Staunton Professor of Psychiatry and Pediatrics at WPIC whose research centers largely on the emotional turmoil that characterizes the teenage years, says Luna's work has been especially exciting for him and his colleagues. He likens the motivations and passions of adolescence to a ship's engine and the cognitive control to the wheel. Although cognitive control is responsible for steering the ship, it's always been a very hard thing to measure, both in the physiology of the brain and in its link to behavior.

“Bea is measuring not just the ability to inhibit behavior,” he says, “but also the ability to make yourself do something that overrides an impulse—and to do it quickly, accurately, and precisely. I think that's a really unique slice that is going to leverage a whole lot of investigation that has relevance to boost clinical interventions and social policy interventions.”

Yet another disorder Luna's work speaks to is attention-deficit/hyperactivity disorder, a condition that affects response inhibition. In a preliminary study led by Irene Loe, a postdoctoral research scholar at Children's Hospital of Pittsburgh of UPMC, the team has already found encouraging results. Within the ADHD subjects who've been tested so far, the researchers are beginning to identify subgroups with common circuitry that are better at cognitive control than others.

“ADHD is a serious health problem,”

says Asato. “A lot of these individuals don't make good choices and may not ‘grow out of it.’ In some cases, because of other psychiatric comorbidities, some individuals may be at higher risk of ending up in the criminal-justice system.”

Last December, Luna attended a meeting in Pittsburgh's Garfield neighborhood. It looked like an ordinary PTA meeting—an informal gathering of T-shirted parents and grandparents sitting around a table and drinking coffee. They talked about their organizational newsletter, their Web site, their kids.

But this was no PTA function.

“It was the most humbling meeting I've ever been to in my life,” says Luna.

She was invited to speak at the monthly board meeting for a Pittsburgh-based activist group called Fight for Lifers West. They are family and friends of prisoners sentenced to life without parole for crimes committed as adolescents in Pennsylvania. More lifers have been convicted as juveniles in Pennsylvania than in any other state in the country.

“My child was 15,” one mother said. “Yes, she did something horrendous, something stupid. And now, for the rest of her life, she's going to be in a cell.” Many of the group's members say this punishment is worse than dying. They call it “the living death.”

None of them was crying. Luna could tell

tors, community groups, and fellow parents. Every chance she gets, she shares what she has learned, which is, in a sentence: Adolescence is not a disease.

“Yes, it's easy to get angry when [teenagers] do something stupid, but sometimes that might be the best that they could do. Give them a break. And don't give up on them.”

Luna admits that it's challenging in those I-know-everything, I-don't-care-what-you-have-to-say moments, but giving up means missing out on a valuable opportunity.

“That feedback might result in a better-developed brain,” she says.

Her own son and daughter are bright, good-natured, “amazing” kids, reports Luna. Both are honors students—at 16, her son has already secured tuition awards for college. But like all adolescents, they have their trying times, especially when they're sleep deprived.



## “What can I say, Mom? I'm not fully myelinated.”

that these parents were seasoned. But as she sat listening to their stories, thinking about the cold, hard facts—sentencing at 16, life expectancy of 70-plus—it was almost too much. “I literally had to hold back the tears,” she says.

Luna gave her presentation to an attentive audience. The families responded with enthusiasm, thanked her, and extended an open invitation to future meetings. “I've been so busy, I haven't been back,” Luna says with a sigh.

Between working at her lab, reviewing grant proposals for an NIH study section, mentoring young researchers, answering reporters' questions, unlocking the mysteries of the adolescent brain, and raising two specimens of her own, there isn't nearly as much time for community involvement as Luna would like. She does her best, though, voicing her concerns to public-school administra-

They can be slow to clean their rooms, quick to argue, stubborn, and unwilling to listen.

It isn't easy being one of the few parents in the world who truly knows so much about what's going on inside a teenager's brain. Your kids do eventually catch on and use the science against you.


“Just recently my son was doing it again,” says Luna. “He was tired and was getting particularly moody—reactive. And I'm like, ‘Have you done your homework?’ We had a little fight, so the next day I was like, ‘You know, that's not how we should talk to each other.’ And he's like, ‘What can I say, Mom? I'm not fully myelinated, and you should understand that by now.’”

“So I said, ‘Yes, but part of you myelinating correctly is that I tell you when you cross the line.’” ■









THE LOEBERS BEAR WITNESS  
TO GENERATIONS OF KIDS SWEEPED  
AWAY BY TROUBLED TIMES  
BY JOE MIKSCH

# CRIME SCENES

**R**olf Loeber and Magda Stouthamer-Loeber seem naturally inclined to take the long view.

They have been married for 40 years. The Pittsburgh Youth Study, their investigation into the causes of juvenile delinquency, has consumed two of those decades. The study has produced 138 papers involving 50 authors, as well as a handful of books.

In 1991, Magda, a PhD associate professor of psychiatry and psychology at the University of Pittsburgh, developed an itch to read as much 19th-century Irish fiction as she could find—"I'm always reading. I like almost any book. I'm not a picky reader," she says.

PHOTOGRAPHY | JIM JUDKIS

Rolf—who, like Magda, is Dutch—has an affinity for things Irish. (While pursuing a master's degree in psychology in the Netherlands, he published a book of Irish stories he translated into Dutch. After getting his PhD in clinical psychology at Ontario's Queen's University, he published a biographical dictionary of 17th-century Irish architects.)

So he prepared a four-page reading list for Magda.

By 2006, that list had grown into a four-and-a-half-pound, 1,500-page book titled *A Guide to Irish Fiction, 1650-1900*, which, according to the London *Times Literary Supplement*, is “set to become the text on which subsequent studies of written and printed fictions in Ireland will inevitably, and gratefully, be based.”

Their motivation to assemble the first compendium of Irish fiction since 1985? Simple curiosity.

“Magda read [the books on the list] and said, ‘There must be more,’” says Rolf, a Distinguished Professor of Psychiatry at Pitt.

“I like these challenges, and I said, ‘Perhaps I should really try to answer that.’ And we started digging.”

They uncovered 5,889 titles written by 1,455 named authors and 286 anonymous scribblers.

“We found a huge number of new authors,” Rolf says, before correcting himself. “Well, what I mean is new old authors. The last major compilation of Irish fiction was years ago, and it was clear there was much more out there. We found it.”

The Loebers live in a capacious apartment off South Highland Avenue in Pittsburgh's Shadyside neighborhood. Both are tall, thin, and gracious. During a recent visit, the Loebers sit in their living room, eager to discuss their work. Rolf notes that the couple is in the midst of another longitudinal study, the Pittsburgh Girls Study—a companion to the Youth Study, which focuses solely on boys. Before delving too deeply into the study, the Loebers point out another of their interests: collecting art and antique furniture. (Magda says the couple eschews a particular style, buying whatever charms them.)

A statue that dramatizes a scene from the 1889 Johnstown Flood stands in front of the fireplace. It shows a woman, holding a child, standing on a steeply pitched roof as the water reaches for her feet.

“It was covered in gold spray paint,” says Rolf. “We cleaned it, and there was gold leaf underneath.” A lucky find. But when the

Loebers turn to their work, they are precise and thorough, leaving much less to chance.

Since 1987, the Loebers have followed the lives of about 1,500 Pittsburgh boys, gathering data from one-on-one interviews, from teachers, and from parents. The planning process began in 1983; at that time, Rolf says, he and Magda decided that the project had to incorporate as many subjects as possible if they were to get the clearest possible data. The more participants and the longer the study lasted, they reckoned, the better they could trace the causes of crime, the peak ages for criminal activity, and how contributing factors vary with age.

When the Pittsburgh Youth Study began, the Loebers' recruits were 7, 10, and 13 years old and from a cross-section of Pittsburgh's population. Study researchers conducted regular follow-up interviews with the boys, as well as with family members and teachers. They also checked regularly with the courts. Before proceeding, the Loebers knew that serious criminal activity among youth peaked in adolescence, with many juvenile offenders returning to something approximating the straight and narrow in their early 20s. What was less well understood were the factors that, say, contributed to one generation of 17-year-olds being more criminally inclined than another.

“The age-crime curve is a universal phenomenon,” Rolf says. “Crime tends to peak in late adolescence. But the height of that peak, and how long people will be engaged in crime, is not fixed. So we acted and became the first study to document the age-crime curve over time for different ages of several age cohorts.”

Economic factors, national crime trends, neighborhood stability and safety, and levels of gang membership, gun ownership, and drug dealing, the Loebers confirmed, varied over time, accounting for rises and falls in criminal activity among youth.

These larger societal factors might be thought of as a rising tide lifting all boats, but for the worse.

The early '90s, Rolf says, were particularly rough. Crime was on the rise in many Pittsburgh neighborhoods. Members of the oldest cohort were in their late teens, an age when criminal activity reaches its peak. They ended up with longer and more vigorous “criminal careers,” Rolf says.

“When the youngest group was at the same age, there was much less crime among them.”

Magda says one of the great surprises of the study was the level of violence young people engage in and are subject to.

“We had 33 homicide offenders in the total sample,” she says. A similar number of participants were homicide victims. “We severely underestimated the amount of violence we'd encounter with the [oldest] sample,” she adds. “Part of that had to do with the fact that no one could have predicted that, over the course of the study, the crime rate would rise in the city. The older kids in particular—when they were in their late adolescence—they were swept up by violence.”

“Before our work, the knowledge about homicide offenders was limited to case reports, what comes after the fact—a kind of reconstruction,” Rolf adds. “What we have is information from different sources, including the boys themselves and parents and teachers, as to what happened to these individuals before they committed horrendous crimes.”

The Youth Study data were used to generate a 2005 paper that Rolf calls “one of the first to tell us, prospectively, what are the predictors, not only of violence, but of homicide.” Recent work focuses on pulling factors from the data that tend to reduce criminal behavior among youth.

Empirical studies show that many of the known predictors of violence and homicide, such as parents' poor child-rearing practices and children's poor impulse control, can be modified, resulting in lowered antisocial behavior and lowered risk for violence.

From the living room, down a narrow corridor, to the Loeber library. A bust of George Bernard Shaw stands sentinel atop one of a seemingly endless supply of bookshelves. He appears deep in thought, perhaps wondering what became of the 2,000 Irish fiction titles the Loebers sold to the University of Notre Dame Irish collection. Students of Irish fiction at the South Bend, Ind., school not only use the Loebers' books as resources, but also the Loebers themselves, relying on their expertise for their dissertations. “It's actually quite enjoyable, not that I can answer all their questions,” Rolf says with a smile.

A massive antique table is barely visible under piles of books and papers. More bookshelves line the walls of an adjoining room, which is separated from the other by an aged, roll-up map of Ireland. The chaise lounge, which resembles the archetypical psychiatrist's couch, is where Magda did most of her reading. Rolf sat next to her and listened as she read aloud, taking the notes that would become the *Guide's* plot synopses.

In the first 115 pages of the resulting tome, the Loebers, scholars that they are, offer a key to abbreviations, spell out their methodology,





ABOVE: Rolf and Magda Loeber relied on a personal collection of thousands of volumes of Irish literature, including *Harry Lorrequer*, and a decades-long interest in the subject to compile their 1,500-page *A Guide to Irish Fiction, 1650-1900*. RIGHT: Careful reading by Magda yielded plot synopses for more than 900 of the 5,889 entries in the couple's catalog of Irish lit.



and outline their key findings. The remainder of the book is broken down into sections attending to the anonymous authors of one work, anonymous authors of multiple works, and the works of known authors. The back of the book indexes people, titles, historic periods, themes and settings, publishers, and places related to authors.

Regarding the *Guide's* thoroughness, Rolf notes that the book should be regarded as more of a social and political history of Ireland than a survey of Irish literature.

"For us it was not [about] discovering the best Irish writer. It was about social history," he says. "What people wrote pertained to the development of political ideas, cultural ideas, and that's what we wanted to report."

Fiction, it seems, is merely a means to an end. "I'm interested in what happens to nations," he says. "How did a country that's basically a colony become independent, and to what extent does that involve a change in culture? Over time, there has been a merging of culture [Gaelic v. English, Protestant v. Catholic], so

I'm interested in what the barriers are to that evolution, or why it's flourishing."

A certain topic might have resonated in a particular literary time, notes Rolf, pointing toward the 19th century and the dawn of the Industrial Revolution for examples.

"At that time, there [were] a number of different genres regarding the welfare of different groups, social issues," he says. "It could be individuals living on farms, poor tenant farmers living in hovels. It could be about tenements, chimney boys, prostitutes. There was a huge body of literature that tried to reduce levels of drinking. There was an evolution of different forms of literature that tend to be reforming, that try to help people get better."

Centuries later, social welfare instincts are alive and well among the Loebers.

In concert with the City of Pittsburgh and several foundations, the couple has advanced the adoption of an intervention program

directed toward reducing the risk of delinquency in pre-adolescent boys.

"The under-12 group is a particularly underserved group of children," Rolf says. "When they violate the law, police find them and bring them home, but not much happens." The Loebers and the city are taking bids from social service agencies interested in guiding the program.

When the couple started the Girls Study in 1999, they suspected that the precursors of antisocial behavior in girls might be different from those preceding delinquency in boys.

To get started, the Loebers hired a cadre of assistants who spent about a year knocking on the doors of 103,238 households in Pittsburgh. They needed girls between 5 and 8 years old, and the study staff identified 2,451.

They are still collecting data, Rolf says, but the study has thus far "made it clear that what applies to boys [in terms of delinquency] only partially applies to girls.

"With girls, we've seen more anxiety and depression, more comorbidities and concur-

ring problems." Delinquent girls also exhibit higher incidences of antisocial personality disorder and substance abuse.

As with the Youth Study, the Loebers rely on annual face-to-face interviews with participating subjects, as well as conversations with parents and teachers.

"Next to nothing is known about the etiology of those comorbid girls," Rolf says. "We are looking to change that."

He is optimistic that the Girls Study will spawn quality data to guide other researchers. The integrity of the sample, he says, is key. Since the study began, it has retained about 95 percent of the original participants. Magda credits this rate to their practice of relying on a corps of helpers they train and pay, rather than hiring outside contractors to collect data. "We have more control," she says. "We set up internal checks so we would know if something went wrong, and when it went wrong." Both note that Pittsburgh itself is a benefit for researchers doing long-term work. "Pittsburgh is great compared to other major cities. This is such a stable population," says Magda.

"Most people who watch TV think about crime as something intriguing, and that's the way TV presents it. Of course, it is intriguing, but I don't find any romance in it," Rolf says.

"Our mission is to try and figure out the causes of violence in a community and the parameters through which we could actually bring about change."

One last visit to the Loebers' library reveals a pile of books on a small table in a corner. Magda carelessly remarks, "Oh, we still need to catalog those."

But isn't the *Guide* done? What's left to catalog?

"Well, we're working on a guide to Irish poetry and songs," she responds.

It seems that retirement, or even slowing down, isn't in the Loebers' plans.

"As long as I can still contribute to science, I'll keep working," Rolf says. Growing more excited, he notes that a great deal of data from the Youth Study remain to be digested.

"And the Girls Study is building up," he adds with a grin.

Regarding the nascent guide to Irish poetry and song, Magda seems to approach it as a serious diversion, if there is such a thing.

"It doesn't even really matter if we finish it," she says. "We can quit. We can persevere. It doesn't matter. It's just an enjoyable thing to do," she says. "It's all very exciting. It's a good life." ■





SCIENCE SHINES A LIGHT ON THE INJURED  
BRAIN OF A CHILD | BY CHUCK STARESINIC

# INSIDE THE BLACKOUT

About 10 years ago, a 14-year-old boy—we'll call him Cedric—was hit while riding his bicycle through a Pittsburgh-area neighborhood. Even after all this time, it's not known how the accident happened. If there was a witness, that person never came forward. The driver of the vehicle that collided with Cedric apparently fled the scene and has never been identified.

"The bike was all bent up, and he was thrown 30 feet," says neurosurgeon David Adelson, director of pediatric neurotrauma at Children's Hospital of Pittsburgh of UPMC. "It was a horrible injury. We had him in a coma for three or four weeks, and we were doing everything.

"But he was hemorrhaging, and the family was distraught. They were even talking about withdrawing care."

The devastating thing about brain trauma, says Adelson, is that a child can be perfectly healthy one moment and fighting to stay alive the next. And it happens all the time—on average, a child sustains a traumatic brain injury (TBI) serious enough to cause permanent disability every 11 minutes in this country. Trauma kills more children in the United States than all other causes of death combined. The biggest culprit is TBI, which kills about 7,000 children each year.

Disability from head trauma ranges from memory and cognitive deficits to vegetative states. Despite the enormous toll, there has been almost no pediatric clinical research in TBI. Children are treated as “little adults,” though their brains are different. And unlike other diseases, there are few foundations advocating for a breakthrough or funding research.

In part, it's a failure of imagination. It's easy to picture a breakthrough cancer drug or an AIDS vaccine. But isn't head trauma primarily a prevention problem, to be solved by a better helmet or a reduction in traffic accidents?

Prevention may be of paramount importance, but physician-scientists at the University of Pittsburgh believe science can do a great deal to change the outcome for the child with TBI. And they are uniquely located to shepherd discoveries from the lab to the intensive care unit.

The National Institutes of Health made an effort in the 1990s to create several centers of excellence in TBI research. Not all of them have thrived and diversified as Pitt's has, says David Hovda, neurosurgery professor at the University of California, Los Angeles and director of UCLA's Brain Injury Research Center.

“What really puts Pittsburgh on the map, with the Medical College of Virginia and probably UCLA, is there are now very few that have both funded clinical and basic science research programs. And there are only two of the original NIH centers that I'm aware of—Pittsburgh and UCLA—that have funding in pediatric traumatic brain injury.”

Robert Clark (Fel '95), Pitt associate professor of critical care medicine and pediatrics and a critical care physician in Children's ICU, says that two or three decades ago, children with lung or heart disease, shock, or overwhelming infections frequently died in the ICU. Back then, he says, “people would have thought that if, by 2006, we could get our ICU mortality around 3 percent, that we were dreaming. But nowadays, it's a reality.”

Adelson and Clark are trying to bring TBI

mortality in line with these other diseases. Their work in this regard can be traced to the epicenter of TBI work at Pitt—the Safar Center for Resuscitation Research.

The Safar Center is a plain block of laboratory space on Pitt's medical campus. Its vigor lies in the network of physician-scientists who commit a large portion of their professional lives to working in these labs but who also cross the street and care for patients in emergency rooms, trauma bays, and ICUs. For these docs, the name of the game is neuroprotection. And there are two questions to be answered: What are the processes that lead to brain damage in the trauma victim? And how do we mitigate that damage?

Adelson's office at Children's is a small, windowless room lined with floor-to-ceiling bookshelves. On a high shelf behind where he sits is a large teddy bear wearing surgeon's scrubs—the lone indication that this is the office of a pediatric neurosurgeon.

Adelson describes the treatment Cedric received in the ICU a decade ago: “We had pressure monitors in [the skull]. We were draining off cerebrospinal fluid and giving different medications to reduce swelling.”

The boy was comatose and on life support for weeks when the parents began to wonder about turning off the respirator. Adelson, now also a Pitt endowed professor of neurological surgery and director of the Walter L. Copeland Laboratory for Neurological Research, remembers how he and other physicians in Children's pediatric ICU told the parents that it wasn't yet time to make that decision. *He is not in any pain, they said. We have him medicated so that he remains in a deep coma.* (His injuries were serious enough to put him in a coma. Doctors believed that keeping him there would give him more time to heal.) *Let us try to stabilize him and see if that will control the damage that is occurring in his brain. Then maybe we can begin to wake him up and see where we are.*

This is the blackout period. In serious brain trauma, it can last a few days, or it can stretch much longer. There is no communication with the patient and little objective information that doctors can use to determine the severity of the injury or what the ultimate outcome might be.

The blackout period is one way in which brain injury differs from so many other traumas and diseases being treated in the pediatric ICU.

The blood brims with chemical information—proteins, enzymes, acids, hormones, immune cells—all of which can provide specific details about what is going on inside the body of a patient, even one who is comatose. By analyzing the blood, doctors can tell not only whether the liver, lungs, immune system, heart, or kidneys are malfunctioning, but also the physiological and molecular details of how they might be failing. Depending on the results, there are multiple medications, interventions, and therapies available. Doctors can monitor changes by the hour, or even by the minute, and change treatments accordingly.

Not so with the brain.

After the initial rush to stabilize Cedric and deliver him to the ICU, parents and doctors were met with weeks of radio silence. The doctors tried to control the bleeding and inflammation in his skull to reduce the secondary effects of the brain injury. The initial trauma doesn't cause the greatest damage. The primary insult—say, a bruise in the brain—sets up a biochemical cascade of events contributing to further inflammation and cell death.

Inflammation is the body's reaction to injury. In your joints and limbs, it's usually not a big deal. It even aids the healing process in ways. Inflammation has some healing benefits in the brain, too, but uncontrolled swelling inside the cranium can wreak havoc, causing irreversible damage and even death.

“The skull is a closed box,” says Adelson. “Unlike the ankle, where you get a big puffy purple ankle, the brain is a closed system, so if it swells, then blood flow going in is decreased.” The brain becomes starved for oxygen, leading to additional injury and cell death.

The tools available to treat TBI are still limited. As they did with Cedric, doctors try to reduce intracranial pressure with medication and by draining cerebrospinal fluid. If this doesn't work, neurosurgeons may perform a decompressive craniectomy, removing a plate of bone from the skull to allow the brain room to swell. When the swelling decreases, the bone is replaced, perhaps several weeks later.

As part of a new clinical trial, children with traumatic brain injuries who arrive at Children's Hospital of Pittsburgh and 11 other hospitals in the country will now have access to an experimental therapy that induces hypothermia. Adelson is the principal investigator on this \$14 million, multicenter trial funded by an NIH grant.

A child with TBI who is enrolled in the study is randomly assigned to receive either hypothermia or standard care. In those tagged for



hypothermia, doctors push cold fluids through their veins. They wrap them in cooling blankets to further lower core temperature and keep it low for two or three days.

This is the blackout period on ice.

"The goal is to cool down early and rapidly, within six hours of the injury," says Adelson. "From there, we lower the body temperature down to 32 to 33 degrees centigrade, which is about 89 to 90 [degrees Fahrenheit]. That is a temperature that is cold enough that there is probably a good effect but it doesn't have the complications. Once you get down to 29 to 30 centigrade, then you start having problems—

arrhythmias, heart problems, coagulopathy, which leads to increased risk of hemorrhaging and infection. The body tends to shut down."

The treatment is experimental, but Adelson has already led a Phase II study with 75 children that demonstrated it was safe. The Phase III study aims to extend those results with the treatment of an additional 400 patients. By cooling, he and his colleagues believe they will reduce inflammation and thereby reduce the chemical cascade that leads to further cell death and damage.

"The preliminary data [from the Phase II study] showed that we did decrease mortality.

In the group that was cooled, mortality was 5 percent, versus 17 percent for those that were not," says Adelson.

If that trend holds up, hypothermia would be a breakthrough.

"This is probably one of our best chances at having something work," says UCLA's Hovda. He cites a long history of evidence leading to this promising trial, beginning with old news reports of children falling through winter ice into lakes and remaining under water for long periods of time—yet recovering completely.

Patrick Kochanek, Pitt professor of critical care medicine and director of the Safar Center,

## ABUSE: THE HIDDEN EPIDEMIC

### SCIENCE OPENS THE DOOR TO A DARK ROOM

When they come into the ER, shaken babies may show symptoms such as vomiting, irritability, or listlessness, but little else. That can make accurate diagnosis difficult.

If a parent shook the baby, he or she isn't going to admit it. If the babysitter did, the parent probably wouldn't know about it.

Rachel Berger remembers attending a series of morbidity and mortality conferences as a pediatrics resident. Hospital staff had sent home three infants with vague symptoms. Each returned within weeks, in critical condition. Two died; one lapsed into a persistent vegetative state.

They were shaken babies—victims of abuse. Yet despite multiple exams by pediatricians with decades of experience, none was accurately diagnosed in time to avert subsequent injury or death.

"Inflicted brain injury is one of those diseases that nobody thinks about but is actually fairly common," says Berger (Res '99, Fel '01). "The incidence of muscular dystrophy is about one in 4,000; they have a national telethon. It's about one in 3,000 for babies under 12 months with inflicted brain injury—fatal or severe. That doesn't even include any mild or moderate [cases].

"There's very little public attention to what is now rapidly becoming one of the leading killers of babies," she notes, as deaths from sudden infant death syndrome decline.

As a pediatric fellow, Berger, now a Pitt assistant professor of pediatrics, started moonlighting in the ICU at Children's Hospital of Pittsburgh. There, she met Patrick Kochanek, director of the Safar Center, professor of critical care medicine, and attending physician.

Kochanek had learned a thing or two about child abuse in two decades of brain trauma research. In the mid-'90s, a colleague began measuring the levels of excitatory amino acids in samples of cerebrospinal fluid from children. The levels were high in infants with brain injuries, says Kochanek. In shaken babies, they were off the charts.

And unlike the babies with accidental injuries, whose levels started high and tapered off, the shaken babies had levels that rose for days.

Another study from the Safar Center looked for molecules in cerebrospinal fluid known to spike in adults within three or four days of a brain injury. Shaken babies had chronically high levels of the molecules.

Yet when Berger suggested to Kochanek that they look for markers of brain injury in the blood of abused infants, his response was tepid.

"Well, the blood is kind of far from the action," he told her. "The blood-brain barrier keeps things out. You'd have to be lucky. These markers would be in incredibly small amounts."

To persuade him, Berger delivered a large box of European studies

that used blood biomarkers of brain injury in adults. Unlike cerebrospinal fluid, blood is routinely drawn, so a reliable test for signs of head injury in the blood could help diagnose a lot of children.

Kochanek conceded it was worth a try.

The result was a paper identifying three biomarkers for head injury in children—proteins released when different components of the central nervous system (neurons, myelin, and glial cells) die or break down. They apparently squeak across the blood-brain barrier in nanograms per milliliter, just enough to detect.

Next, they looked for the biomarkers in infants with symptoms such as unexplained vomiting. For reasons such as cost and sheer numbers, it's just not practical to do head scans on all such babies.

Fourteen out of approximately 100 of the babies were diagnosed with a head injury. (Berger's test was used for research only, not diagnosis. The blood was banked and studied long after the infants left the hospital.) Eleven of the 14 had elevated levels of the biomarkers. If the blood test had been part of the clinical care protocol, says Berger, it would have prompted head scans in those patients.

Another five were not initially diagnosed with a head injury, but were back in the emergency department as victims of abuse within six months. Berger revisited their blood work and found that four had had elevated levels of the biomarkers when they first came in—a clue, perhaps, to brain injury at the time the blood had been drawn.

The criteria seem to work, says Berger. About 6 percent of children in that initial study came back to the hospital identified as abused children: "That's an incredibly high percentage," she says. "We picked the right population to screen."

The next study is already under way, with funding from the Pediatric Clinical and Translational Research Center at Pitt. Berger and colleagues will enroll close to 1,000 babies in Salt Lake City and Pittsburgh who show symptoms that could suggest brain injury, such as vomiting and fever. Each will have a head scan and blood work to measure biomarkers. The study will follow them until they turn 1.

For parents, the specter of a false accusation of abuse is a frightening prospect. But Berger and others in the field say these tests will never reach the level of a definitive diagnosis.

"What she's advocating, which is a wonderful idea, is a way to see which children need to be further screened for head trauma," says Carole Jenny, a professor of pediatrics at Brown University.

You can't put every child with low-grade fever and vomiting into the scanner, says Berger, so better tools for screening are a must. —CS

says the first experimental example of hypothermia's benefit in head trauma came from a Safar Center lab pediatric experiment more than 12 years ago. In that study, short bursts of hypothermia led to improved outcomes in young animals with head injury. Years later, Pitt researchers conducted an adult hypothermia trial. That indirectly led to Adelson's clinical trial.

The adult trial was stopped early. It was clear the benefit was not going to reach statistical significance, says Adelson.

"But when they went back to look at the data, what they found was that older patients, those over 40 years of age, didn't do well. In fact, they did worse with the hypothermia. Those under 40 did better. Now that was only a trend, but that gave us an indication that perhaps children would do even better," he says.

Every day that Robert Clark is on the job as an attending physician in Children's ICU, there is at least one child with a traumatic brain injury. It could be a child who was in a car accident that morning. It could be a child who has been in a coma for several days. But always there

his lab. It gave him a chance to show that the mechanisms and pathways of cell death and injury he'd observed in the lab were present in humans, too.

"What he did," says Kochanek, "was to link the molecular lab work directly to traumatic brain injury. Everybody quoted it."

Researchers have long noted that boys tend to have worse outcomes in terms of intellectual performance after head injury. Boys and girls also express cytochrome C—a protein prominent in the apoptotic cell-death pathway whose effect is targeted by hypothermia and some drug therapies—differently after brain injury. Right now, in the ICU, boys and girls with TBI get the same treatment. Clark thinks that should change.

He believes that different patients need different treatments. His vision is to tailor drug therapy to individual patients based on gender, age, genetics, and where in the brain the injury occurred—something that doesn't happen much in the ICU today.

TBI can eventually kill brain cells in many different ways, notes Clark. TBI's partners in crime are different proteases, lipases, and other destructive enzymes, some of which appear to

narcotics, and antiseizure medicines, as well as cytokines and toxic byproducts of cell injury. The efficiency of these various pumps helps determine not only the level of medication in the brain but which types of cell damage are most dangerous for a specific patient.

"I'm envisioning in the future being able to get a profile of everyone—age, gender, genotype, and very sophisticated neural imaging that shows where the potential areas of damage are," says Clark. With a complex understanding of each patient, the types of damage occurring, and the process of recovery, doctors could use direct, targeted therapies to treat patients.

"Maybe 10 years from now," he says hopefully.

That's why Adelson's hypothermia trial is so important, Clark says.

"I think we've got to do it now," Clark says.

"Hopefully, 10 years from now, we won't need it. But right now we've got nothing else. And there's nothing else that I'm aware of in the pipeline that's ready to go tomorrow."

Both of these doctors can tell stories of patients and families who never recover what they've lost to a traumatic brain injury. But both are regularly inspired by what Adelson calls the "immeasurable reward" of seeing a child bounce back from what appeared to be a devastating injury. These are the people they think of when they describe the importance of increasing positive outcomes, even by a few percentage points at a time.

Recalling Cedric, Adelson says, "That kid pulled through. He was in rehabilitation for six months. But that kid has graduated college now. When you talk to him, he doesn't have any deficits that you can tell. He has a little bit of memory and cognition issues. He has to work a little bit harder, but he graduated from Penn State."

Clark describes a similar experience with a wry twist. He had a patient who was in an accident on an all-terrain vehicle while not wearing a helmet.

"He had a bad head injury," says Clark. The boy couldn't talk and couldn't walk. The father was by his side every day in the ICU. He told his son that as soon as he could walk, he would buy him a motorcycle.

"The dad came back a year later with a picture of the kid next to his motorcycle," says Clark. "I do think he had a helmet in hand."

Clark acknowledges that the boy is not a poster child for prevention. "But God bless him. He left the ICU, and we had doubts that he would be neurologically intact enough to ride a motorcycle." ■

## He cites a long history of evidence, beginning with old news reports of children falling through winter ice into lakes and remaining under water for long periods of time—yet recovering completely.

is someone. Clark is painfully aware of the dearth of clinical trials in pediatric TBI.

"I've been doing this since 1995. There is less variation in treatment now," he says, from hospital to hospital and doctor to doctor. "It's more protocolized. But there have been no breakthroughs."

Clark is quiet and unassuming, with pictures of his two daughters lining the tops of the bookcases in his office at the Safar Center. But he is intense about his work.

"Bob Clark published 11 papers as a fellow, if you can imagine," says Kochanek. "He had multiple R01 [NIH research project] grants—a huge success story."

After his critical care medicine fellowship at Pitt, Clark studied mechanisms of cell death in neurons in the lab. But his cell cultures were a world away from the brain-injured patients across Fifth Avenue in the ICU. To reduce intracranial pressure, ICU staff drained and discarded their patients' cerebrospinal fluid. Clark started to bank this fluid and study it in

be more prominent depending on the gender of the patient. Some are more prominent in an abused infant than a 16-year-old who has been in a car accident. An injury to the hippocampus is different from an injury to the cerebral cortex. Timing makes a difference, too. Mechanisms of injury immediately after the initial insult are different from those seen 12 hours later.

Clark's lab investigates a gene for P-glycoprotein, a receptor on the blood-brain barrier that helps pump molecules out of the brain. He has found that if you have a specific, subtle genetic variant, the efficiency of that pump will vary. Most of the time, "that's not a big deal," he says. "But when you are under duress—you've got an injury, and you are getting a bunch of medications that you've never seen before—the efficiency of that pump becomes much, much more relevant to how you respond to those medications."

There are many such receptors in the blood-brain barrier. They pump out analgesics,



*People and programs  
that keep the school  
healthy and vibrant*



## NOBLE INTENTIONS

### JOSEPH DICKSON PRIZED SCIENTIFIC ACHIEVEMENT

BY MATT MINCZESKI

Joseph Dickson (MD 1893) used to sit at his desk in his home in suburban Pittsburgh's Mt. Lebanon and labor over calculus and algebraic equations—when he was in his 80s and long retired.

"That's how he was. He was erudite, an intellectual," says Sylvester Stoehr, a family friend.

When Dickson died in 1954, his will and that of his wife, Agnes Fischer Dickson, stipulated that their estates endow a trust to fund the Dickson Prize in Medicine at the University of Pittsburgh and the Dickson Prize in Science at Carnegie Mellon University. Each is awarded annually to a person who has made outstanding research contributions. The first Dickson Prize came with a \$10,000 stipend; today \$50,000 accompanies the bronze medal.

The Dickson Prize is the School of Medicine's highest award, and it often presages other major accolades. Since 1969, 11 Dickson winners have gone on to win Nobel Prizes, including Phillip Sharp, who won the 1990 Dickson for his discovery of split genes.

"It was one of the early recognitions of the importance of that research," says Sharp, who received the Nobel in 1993. "It certainly did elevate me in the eyes of the institute I was a part of, MIT."

"The Dickson is comparatively young contrasted with the Nobel," says the 2006 recipient of both awards, Roger Kornberg, of Stanford University, who was honored for his findings on gene regulation and transcription. "But it's administered by a very fine group of scientists whose professionalism is widely respected, and their choices have been favorably viewed by the scientific community. Over the years, the prize has garnered respect."

Dickson was born in Mansfield Valley, Pa., now Carnegie, in 1868. He graduated from Washington & Jefferson College in Washington, Pa., Mount Union College in Alliance, Ohio, and the Western Pennsylvania Medical College (now the University of Pittsburgh School of Medicine). He also trained in surgery at St. Bartholomew's Hospital in London and St. Louis Hospital in Paris. Dickson eventually settled in Pittsburgh and started a practice downtown on the corner of 9th Street and Liberty Avenue. His son and only heir, James Dickson, died of Hodgkin's disease in 1923 at the age of 16.

Stoehr still refers to the Dicksons as "Uncle Joe and Aunt Agnes." They were unrelated, but Stoehr's father was Dickson's good friend. Dickson performed a life-saving emergency surgery on the younger Stoehr, removing his (literally) bursting appendix in 1931, when Stoehr was 11.

"He told me that it cost more to clean up the operating room than it did for the operation," says Stoehr.

Stoehr will always remember Dickson as "the uncle who saved my life." Dickson's generosity has influenced medical science to an extent he may never have imagined. ■



Pittsburgh physician Joseph Dickson and wife Agnes Fischer Dickson "had a vision of progress," the *Pittsburgh Post-Gazette* declared. Today, their prize presages greatness.

## BOOSTER SHOTS

If you're trying to get in touch with **Ron Salvitti** (and if you're not a patient), you may have to wait until 9 p.m. or so. It's a hard-and-fast rule with Salvitti—the workday is for patients. He traces principles like this back to his days as a Pitt ophthalmology resident and chief resident. Mentoring sessions with department chair Dennis Richardson sometimes stretched into the early morning, says Salvitti (Res '73). As a way of thanking the institution where he received his professional training, Salvitti, who practices in Washington, Pa., has established the E. Ronald Salvitti M.D. Chair in Ophthalmology Research.

While members of the Parkinson's disease support group filed out of St. Barnabas Health System's Valencia Woods Nursing Center in Valencia, Pa., **Tony** and **Judy Achkio** talked with the guest speaker, Michael Zigmond, a Pitt professor of neurology. They explained that Tony Achkio was diagnosed with Parkinson's 11 years ago. Zigmond invited them to tour his lab and talked about his research into how exercise increases the brain's protection of the neurons that die during Parkinson's. The Achkios recently gave \$100,000 to support Zigmond's research. —MM

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# NOT ON A SCHOOL NIGHT, OR THE PATH TO LEADERSHIP

FEMALE MED STUDENTS WONDER WHAT'S NEXT FOR THEM

BY HATTIE FLETCHER



Sally Carty's first reaction on being invited to talk about women leaders with University of Pittsburgh medical students at a recent dinner program was, "But that's a school night!" Carty, Pitt professor of surgery and UPMC section head for endocrine surgery, is also the mother of a 9-year-old.

"I'm ruthless about my schedule," she told the aspiring surgeons who had gathered at her table to hear her advice.

The freewheeling dinner conversation was proof (if anyone really needed proof) that women still struggle to balance work and family in the effort to "have it all." "Because that's the thing, right?" Carty said, leaning forward intently. "You want to figure out a way to do both well." She observed that the vast majority of women surgeons marry other surgeons: "You want to be able to discuss your work with your spouse. And also, it's just such a weird lifestyle."

"Women in Medicine: Discovering Your Path to Leadership," presented by Pitt's branch of the American Medical Student Association, was a chance for female med students to chat with Carty and approximately two dozen other women—including deans and department heads—about the experiences and decisions that have shaped their careers.

Anne Docimo, the chief medical officer of UPMC Health Plan and medical director of corporate care management for UPMC, was also at Carty's table. "Hi," Carty said, introducing herself. "I'm Hope's mom." The two had never met but knew of each other through their children as well as their professions.

An evening with professional women talking about their kids and husbands might not have been what the students had anticipated. In that respect, the evening was instructive, especially for the first- and second-year students, many of whom are single and focused primarily on the work part of the work-family equation. They were interested in picking up pointers, sure, but most of the talk around the appetizer buffet concerned first blood draws and the first big test. Indeed, as members of classes that are at least half women, students

might have been excused for thinking, as one student later admitted she had, that "nothing more needs to be done" and that all she would need to do to succeed would be to follow the path forged by women who came before her.

"As an epidemiologist," said keynote speaker Kathy Helzlsouer (MD '79), "I get nervous about focusing on one story, but as a clinician, I know there's a lot to learn from a case history."

Helzlsouer's "case history" provided reminders of how much medicine has changed in a relatively short period of time. Director of the Prevention and Research Center in the Women's Center for Health and Medicine at Mercy Medical Center in Baltimore and formerly a professor of epidemiology and oncology at Johns Hopkins University (where she was one of only three women to hold that title in an epidemiology department of more than 80 faculty), Helzlsouer remembered being asked in a medical school interview (not at Pitt), "Why should I give a space to you? You'll just get married and have babies and drop out." When applying for a fellowship she decided, though not married or planning to become pregnant at the time, to ask about the maternity leave policy. The answer: "We've never thought about that."

Of course, much has changed in the past 30 years. Women still struggle to time their maternity leaves well, but they can generally assume that policies are in place.

In fact, students' questions and comments during a panel discussion following Helzlsouer's address suggested that they were ready for the next wave of medical feminism.

"Do you have any advice about how we can help men support us in our careers and our efforts to become leaders?" asked Otuodita "Enyinne" Ejiasa (Class of '09), one of the program organizers.

"Maybe it's idealistic of me," Ejiasa said later, "but men are our colleagues, too, and it seems like it would be easier to get the things we need or want with their help." The chief planner for next year's event, it should be noted, is Matthew Stull (Class of '10), who organized this year's meeting with Ejiasa.

"I hope to bring more males around to understand that gender equity in medicine is not just a problem women should face alone," he said.

Women still lag significantly behind men in attaining full professorships, administrative positions, chairs, and directorships at academic medical centers nationally. That small number is due, in part, to women's relatively recent entry into academic medicine, said Ann Thompson, Pitt professor of critical care medicine and pediatrics and associate dean for faculty affairs in the School of Medicine. But the rate of increase is lower than the number of women in medicine would suggest. Additionally, she said, the number of women reaching the rank of professor is particularly low.

At Pitt, 40 percent of assistant professors are women; for associate and full professors, the percentage drops to 30 and 20, respectively—numbers almost perfectly in line with national trends, Thompson explained.

Since his arrival at Pitt in 1998, Arthur S. Levine, dean of the medical school and senior vice chancellor for the health sciences, has established several initiatives to support women's professional development. Five women now chair departments (none had previously in the school's 120-year history). He has also changed the tenure-track system for clinicians, making it more transparent, flexible, and realistic for women to advance.

In recent years, Pitt has provided more networking opportunities, including a Sunrise Series (for junior women fellows and faculty), a Women in Surgery group (at the last meeting, Carty told her table with pride, no one talked about men at all, for the first time ever), and events like this student-initiated conference.

"This is great," said Kelly Wanamaker in the dessert line. (Wanamaker was visiting for a year from Drexel University.) "I've never gotten to hang out with women surgeons before."

"Hanging out," "networking"—whatever you call it, the evening supplied plenty of opportunities for it. And well after the presentations wrapped up and the tables were cleared, women lingered to finish their conversations, even though it was a school night. ■



## CLASS NOTES

### '40s

At the Mayo Clinic in Rochester, Minn., **William Parsons** (MD '48) helped pioneer the first drug that successfully lowered cholesterol. In 1955, during his internal medicine residency, Parsons and his Mayo colleagues conducted the first systematic study of how cholesterol levels were affected by nicotinic acid—the vitamin we know as niacin. Their results were published in 1956 in Mayo's nationally distributed journal (now the *Mayo Clinic Proceedings*). In the late '60s, the Coronary Drug Project, an eight-year study sponsored by the National Heart and Lung Institute involving more than 8,000 men, showed that prescription-strength niacin significantly reduced incidences of heart attack and stroke. Parsons says his initial work at Mayo became the basis for his research career in Madison, Wisc., and later in Scottsdale, Ariz. Now retired, Parsons has self-published two books on niacin that help doctors and patients better understand the drug and its side effects.

### '60s

A few years back, **Norman Weinberger** ran his own pediatric practice in Norwalk, Conn., where he joined forces with a family therapist, a social worker, and a child psychologist. Weinberger (MD '66, Res '69) and his colleagues conducted therapy sessions with parents that stressed how family dynamics influenced child behavior and development. He frequently highlighted the father figure in the family. In one instance, Weinberger encouraged a mother to leave her baby alone with her husband on a Saturday morning. She did, and when she returned the baby was wrapped in duct tape. The father had used it to fasten a diaper. She held the baby up and shouted, "You just don't duct tape a baby!" This definitive statement

became the title of Weinberger's book (Warner Books, 1997) exploring child development through the eyes of a pediatrician and parent. Today, Weinberger is an associate clinical professor at Yale University, and he practices at Stamford Community Health Center, a clinic for underserved children.

### '70s

**Eric Kraus** (MD '77) is one of six American coinvestigators of an implantable hearing aid called the Envoy Esteem. He has implanted the device into 20 patients at his private practice in Greensboro, N.C. He describes it as a breakthrough for sensorineural

hearing loss patients, who normally wear conventional external hearing aids. The Esteem is placed under the skin behind the ear, where it interfaces with two of three hearing-related bones. The FDA is still reviewing the device, but it was approved in Europe in July 2006. Kraus has been training doctors from Europe in his office's temporal bone laboratory to perform the surgery. He estimates that the device could benefit millions of people with hearing loss if it is approved in this country.

**Barbara Wilhelm** (MD '79) has published a novel called *Murder Makes the Rounds* (Pemberton Mysteries, 2006). The story is a mystery romance at heart, but Wilhelm slips in commentary on managed care in hospitals. Writing gives Wilhelm a chance to get on a soapbox and express her preference for small, community-based practices. She used a pseudonym so her patients and colleagues at Mountain Springs Medical in Western Pennsylvania won't assume that the murderous plot describes a true story from their local hospital—a thought Wilhelm chuckles over. She'll keep the alias, Mela Barrows Bennett, which was her great-grandmother's name, because she thinks it's a tremendous pen name for a murder mystery. "Besides," Wilhelm says, "it's a nice way to honor my family."

In 1991, gastric cancer forced **Greg Jones** to shut down the family practice he'd built. Rehabbing from double chemo treatments, he could only walk 100 feet at a time and couldn't work—"I was bored out of my mind." At that point, Jones began writing letters and speaking with local officials on how to improve the horse trails around his Eastern Kentucky community. Now, Jones (MD '79) works with congressmen, senators,



Jones back in the saddle

## DUFFERS BREAK 6,000

### A GOOD WALK SPOILED FOR A GOOD CAUSE

**T**he weather was rotten. The same could be said of some of the golf. And at a time of particular crisis, the beverage cart could not be located. Despite the inclement conditions and lack of timely liquid refreshment on this late April Saturday, the eighth annual Pitt Med Golf Outing at Quicksilver Golf Club in Midway, Pa., raised \$6,000 for Pitt med scholarships.

**Matt Kaufman** (Class of '09) organized the event with **Dan Welchons** (Class of '10) and **Rob Klune** (Class of '08). Kaufman golfed with his father, Stuart, and uncle, Mel—all three are accomplished golfers. The same cannot be said for the *Pitt Med* writer who completed the foursome. Kaufman played the chilly, rain-soaked course with skill and precision. Yet none of the foursome, who lost the third-place tiebreaker, or any of the other 100-plus (in number, not age) golfers, could sink a hole-in-one on a water hazard-protected par 3, where a bright yellow Mini Cooper practically begged to be won.

All money raised via the outing—from greens fees, raffles, and donors like UPMC—goes to the Student Executive Council Scholarships and Loans Fund. The fund makes possible the Dr. Edward Curtiss Leadership Service Award. This competitive award, named after Pitt med's late associate dean of admissions and financial aid, is given to





**Surgeon Pituch (third from right)**

and national forest superintendents on developing a \$9 million, 100–150 mile trail. On the job, Jones is the medical director for three ambulance services that cover five local counties. He's assistant professor of emergency medicine at Ohio University, where he is helping to start the emergency medicine residency program that will begin next year. His undergrad education (which included a minor in animal science) comes in handy in more ways than one: He enjoys talking about farming with his patients in this rural area, and he and his wife own a 170-acre horse farm.

## '80s

**Al Hergenroeder** (MD '80) played football for Central Catholic High School in Oakland. On break from attending medical school one summer, he returned to coach wide receivers. When he graduated, Hergenroeder left for a pediatrics residency at Duke University, intending to return home after three years of training. "I was a Pittsburgh guy from start to finish," says Hergenroeder. "But if you wanna make God laugh, tell him your plans." Hergenroeder ended up in Houston, Texas, at Baylor College of Medicine, where he further indulged his love for sports. He started the section of adolescent medicine and sports medicine pediatrics, the first of its kind in the country. He's a professor of pediatrics and the principal investigator for Baylor's Leadership Education and Adolescent Health Training Program. Every fall, Hergenroeder returns to the football sidelines of local Houston high schools to look after young athletes.

## '90s

**Dawn Marcus** (Neurology Resident '90) has published *10 Simple Solutions to Migraines* (New Harbinger Publications, 2006). In her book, Marcus suggests that keeping a daily diary and taking the book's interactive quizzes will help a patient reflect on the possible causes of migraine symptoms. The methods are designed to help patients open dialogues with doctors about the results they've found, possibly leading to more effective treatment.

The chief of oral and maxillofacial surgery for Pittsburgh's Mercy Hospital and Jefferson Regional Medical Center, **Daniel Pituch** (MD '94), is one of three principal faculty members designing a dental implant center at Pitt's School of Dental Medicine. (Pituch got his DMD at Pitt in 1990.) He also serves as an associate clinical professor at the dental school and teaches in the school's residency training program. He's gotten some favorable press of late for his work with two noteworthy patients: Pittsburgh Steelers quarterback Ben Roethlisberger and an Iraqi child who came to Pittsburgh to have a disfiguring birth defect corrected.

## '00s

**Liz Cuevas** (MD '01) assisted in soup kitchens and homeless shelters in Pittsburgh, but it wasn't until she joined Operation Safety Net that she witnessed the vast medical needs of the homeless. She says those experiences strengthened her resolve to dedicate her career to the underserved. She and classmate Patrick Perri married in their fourth year of med school. Cuevas is at the Boston Healthcare for the Homeless Program, developing a curriculum for med school students and grads on the needs of the homeless.

When Cuevas' husband, **Patrick Perri** (MD '01), was at Pitt, he also ventured under bridges and into alleys with Operation Safety Net to bring medical care to the

homeless. Perri sees himself working for a social justice cause rather than charity: "It doesn't matter how or why these people suffer," Perri says, "it's the fact that they *are* suffering. Our primary obligation as healthcare providers is to help alleviate that suffering in some meaningful way." He and his wife matched to residencies at Massachusetts General Hospital to be near the Healthcare for the Homeless program—where he currently practices, mainly as a street physician. He is a Harvard University clinical instructor in medicine on staff at Massachusetts General. Cuevas and Perri saw their family double when they welcomed fraternal twins—a boy and a girl—in February 2006. —*Matt Minczeski*

## THE WAY WE ARE 2007 HONOR ROLL

**G**raduation from medical school is an end to a formative period, but at Pitt's annual senior class luncheon for graduating medical students, it quickly becomes apparent that graduation is an induction, too. Sometime shortly after dessert and coffee, the senior class takes part in its first official meeting of Pitt's Medical Alumni Association. These newest members get a sense of the club they are joining when the MAA presents awards to two distinguished alumni.

**Beth Piraino** (Res '80, Fel '82) received this year's McElroy Award, given annually to a distinguished physician who completed a residency or fellowship at Pitt. Piraino, a Pitt professor of medicine and associate dean of admissions and financial aid, has worked with the MAA to create a scholarship for Pitt med students between their first and second years to experience health care in other cultures. Piraino made the scholarship possible by donating honoraria that she receives from speaking engagements.

The Hench Award for a distinguished MD graduate of the School of Medicine went to **Bertram Lubin** (MD '64), director of the Children's Hospital Oakland Research Institute in California. (See p. 39 for our profile of Lubin.)

By the end of their fourth year, Pitt med students are already accustomed to these rituals—honoring those among them who excel in creativity, diligence, and selflessness. As third-year students, they recognize teaching excellence in Pitt's medical residents by awarding six "Little Apple" awards.

This year, **Michele Odrobina** (Res '07) won her fourth Little Apple in the four years she trained at Magee-Womens Hospital of UPMC.

*continued on page 38*



graduating students with high levels of educational debt who have made significant contributions to the community. This year's winners are **Joseph Barton** and **Jamie Cavallo** (both MD '07).

The tournament's winners represented Pitt's Department of Surgery—clinical assistant professor **Richard Bondi** (MD '64), professor and chief of pediatric surgery **George**

**Gittes**, and residents **Steven Gribar** and **Kevin Mollen**. They finished 5 under par as a team using the event's "best ball" format. They were also the first winners to have their names inscribed on the Pitt Med Cup, which is brand-new this year. —*Joe Miksch*

continued from page 37

"I try to get the students involved. If I can't take them to a patient, I give them something to read," she says.

She's not the only resident at Magee who won a Little Apple. **Susan Lareau** says she recalls her own experience as a med student: "People do a better a job if you tell them what they are doing well."

Plastic surgery resident **Galen Wachtman** (MD '04) thinks he won a Little Apple because he takes time for students. He was also recognized by the Class of 2006 with the Charles C. Moore teaching award for best resident teaching in the Department of Surgery.

Ophthalmology resident and Little Apple recipient **Mike Alunni** strives to create an inclusive environment. "When you are rotating through a bunch of specialties, it's tough to feel like you are part of a team. I try to make the students feel like they are."

Internal medicine resident and Apple awardee **Thomas Conlon** (MD '06) says teamwork makes teaching easier: "When you make a team function well together, it's inspiring."

**John Falcone** (MD '06), who won a Little Apple as a general surgery resident, says that teaching has become a personal passion.

The Class of 2007 handed out its own awards. They honored **Thuy Bui**—the medical director of Pitt's program for health care to underserved populations and a Pitt assistant professor—with the Leonard Tow Humanism in Medicine Award for her compassion and sensitivity. **Lou Ghanem** (MD/PhD '07) won the student award. Says Ghanem: "I think I just cared for my patients and that showed."

**Susan Dunmire** (MD '85, Res '88), associate professor of emergency medicine and executive director of the MAA, won the Golden Apple Award once again. She says Pitt Med grads like her late grandfather, **Harold Mitchell** (MD '21), and her father, **Lester Dunmire** (MD '48)—have always inspired her: "Both of these men showed me how to teach with gentle guidance and respect for the student."

—Meghan Holohan

## IN MEMORIAM

### '30s

**JOHN WUNDERLICH**  
MD '36  
JAN. 25, 2007

### '40s

**GEORGE E. SPENCER**  
MD '43B  
MAY 22, 2007

**C. LEONARD O'CONNELL**  
MD '44

JAN. 14, 2007

**ARTHUR PATTERSON**  
MD '44

APRIL 13, 2007

**JAMES C. HAYES**  
MD '45

JAN. 13, 2007

### '50s

**ROBERT B. STUART**  
MD '55  
SEPT. 13, 2006

**JOHN A. WOODSIDE**  
MD '56  
APRIL 21, 2007

**GEORGE J. CARSTENS**  
MD '57  
MARCH 29, 2007

### '70s

**JOHN GARROTT**  
RES '74  
MAY 13, 2007

### '80s

**WILLIAM STANDING MERTZ**  
MD '87  
MARCH 14, 2007

### '00s

**CARLOS JOSE TORRES**  
MD '06  
MAY 4, 2007

## ELIZABETH ELMER

MARCH 30, 1911–APRIL 15, 2007



Elmer

When she was a young social worker at Children's Hospital of Pittsburgh, Elizabeth "Betty" Elmer was asked to locate the medical records of a child who'd come in with broken bones. The doctor couldn't remember the name, however. Looking through charts, Elmer was stunned to see how many children suffered repeatedly broken bones.

This chance discovery led her to a long career in child abuse research in the Department of Psychiatry at the University of Pittsburgh School of Medicine. She published two books and numerous research papers on the subject.

She died this year at age 96.

Elmer was a relentless advocate for children and families at a time when there was great resistance to frank discussions of child abuse. Colleagues remember her as 5 feet tall and not afraid of anyone.

In addition to her research and teaching at Children's Hospital, Elmer worked in Pitt's Child Guidance Center and helped to found the Parental Stress Center. Family Resources, a Pittsburgh nonprofit that aims to stop child abuse, annually gives a Betty Elmer award to a person who exemplifies her passion for helping families and protecting children from abuse. —Chuck Staresinic

## JAMES McCLENATHAN

JAN. 11, 1922–JUNE 1, 2007



McClenathan

James McClenathan (MD '47) retired from a long career as a navy surgeon about the time that his three sons were in high school. It was 1965, and after years as chief of surgical research and chief of thoracic and cardiovascular surgery at the National Naval Medical Center in Bethesda, Md., McClenathan became professor of surgery at George Washington University School of Medicine and associate chief of surgery at the District of Columbia Children's Hospital (now Children's National Medical Center). He helped launch that hospital's cardiac surgery program, introducing several open-heart procedures there.

One of his sons, James Jr., eventually became his student at GWU. He says that his father, who died this year at age 85, inspired him in myriad ways. The elder McClenathan personally and meticulously prepared for every aspect of his surgical procedures, from anesthesiology to prepping the ICU staff, especially in those early years of the hospital's cardiac program. And he displayed "an almost childlike wonderment at how it was possible to fix these complex pediatric heart problems," says James Jr.

Now a professor of surgery at Stanford University School of Medicine, the younger McClenathan says that his father continued his journal subscriptions long after retirement and always served as a sounding board for him on surgical issues. "There were very few things in medicine that I couldn't ask him about." —CS



## BERTRAM LUBIN ON DISCOVERING SCIENCE

BY MEGHAN HOLOHAN

**T**he 4-year-old lay on his hospital bed awaiting a neurosurgical consult. The boy—we'll call him Bryan—had a misshapen head. His skull was square, with pointed edges. Doctors thought Bryan suffered from a structural cranial defect.

Bertram "Bert" Lubin (MD '64), then a pediatric resident at Philadelphia Children's Hospital, examined Bryan when he arrived at the hospital. Lubin ordered some tests, the results of which would prove important for them both.

More than 40 years later, Lubin was awarded the 2007 Hensch Distinguished Alumnus Award by the University of Pittsburgh's Medical Alumni Association for his accomplishments in hematology, an interest that began with Bryan.

The tests revealed that Bryan suffered from hereditary stomatocytosis—a severe form of hemolytic anemia that causes the bones, especially those in the skull, to expand abnormally.

Lubin gave Bryan a red blood cell transfusion to increase his hemoglobin, but that didn't work. Hematologists recommended removing his spleen. Although Bryan got a little better following surgery, he continued to suffer from anemia.

Bryan's became one of the first well-studied cases of hereditary stomatocytosis, helping physicians better understand how red blood cells transport water and electrolytes. The increased red blood cell production in response to anemia caused his bones to be weak and misshapen.

Today, Lubin is president of the Children's Hospital Oakland Research Institute (CHORI)

in California, where he still investigates blood diseases.

Lubin talks quickly, and his enthusiasm is infectious. He says he was just an average student growing up in Bellevue, in suburban Pittsburgh. His father owned a produce market, where Lubin worked throughout high school and college. After graduating from Washington & Jefferson College in Washington, Pa., he attended the University of Pittsburgh School of Medicine because, he says, it was the only med school to accept him. Lubin's dad wanted him to keep working at the market while enrolled. So Lubin landed a lab research gig. It took up time he would otherwise have been expected to sell strawberries and spinach. He now has more than 250 published papers to his credit.

Lubin joined Children's Hospital and Research Center Oakland in 1973 as director of hematology/oncology and became president and research director of CHORI in 1980. During his tenure, annual National Institutes of Health (NIH) funding at CHORI has increased from \$1 million to \$50 million. Lubin has been the principal investigator (PI) on NIH-funded grants for 30 years.

He coordinated an NIH-supported Pediatric Clinical Research Center and a postdoctoral pediatric hematology training

program. He also serves as PI for an NIH translational science grant affiliated with the University of California, San Francisco, Clinical and Translational Science Institute.

Lubin developed a unique umbilical cord blood storage program for siblings of children who might need a stem cell transplant. The program, the first to be funded by the National Heart, Lung and Blood Institute, provides an alternative to bone marrow transplantation for kids with disorders like sickle cell anemia, thalassemia, and leukemia. It's the first and only nonprofit bank of its kind in the world.

Parents whose children could be cured through cord blood transplants can cryopreserve newborn sibling cord blood to be used in the event that a transplant is needed.

Says Lubin: "We've cured a number of kids following sibling cord blood transplantation."

At CHORI, Lubin also started an NIH-funded undergraduate research program that exposes underserved undergrad students to medical science. Students work on research projects in CHORI labs and write grant proposals. The program is one of Lubin's proudest accomplishments. It accepts only students who have, as he once did, average grades, Lubin quips. Those with top marks, he notes, will not lack for opportunities. ■



A long-time jazz drummer, Lubin still plays at benefits.

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## MONKEY KNEE, FREDDIE FU

In 1991, Freddie Fu (gesturing to the above patient) operated on *Pitt Med* senior editor Chuck Staresinic's knee. (Sixteen years later, Staresinic is still playing sports on the repaired joint.) In June, Fu explored another limb on the tree of life and performed arthroscopic surgery on Johnny, the Pittsburgh Zoo's 12-year-old mandrill monkey.

Zoo veterinarians knew that Fu (MD '77, Res '82), chair of the Department of Orthopaedic Surgery at the University of Pittsburgh, has an interest in knee evolution, so they gave him a call and invited him to see what was ailing Johnny, who had been grabbing and poking at his knee.

Fu discovered that Johnny had a partial anterior cruciate ligament tear. (He also found that his furry patient's ACL consists of three bundles of tissue. Human patients, such as Staresinic, have two.) Fu said a full-on fix was impractical and removed some inflamed tissue in Johnny's knee to reduce the mandrill's discomfort.

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# C A L E N D A R

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the Medical Alumni Association:  
1-877-MED-ALUM, 412-648-9090, or  
medalum@medschool.pitt.edu.

### WHITE COAT CEREMONY

AUGUST 12

3 p.m.

Scaife Hall, Auditorium 6

### MUSGRAVE LECTURESHIP

OCTOBER 12

5:30 p.m.

Magee-Womens Hospital Auditorium

Thomas J. Baker, MD, Speaker

OCTOBER 13

10 a.m.

Scaife Hall, Lecture Room 2

Surgery Grand Rounds

### HOMECOMING WEEKEND

OCTOBER 18-21

Pittsburgh vs. Cincinnati

Saturday, October 20

For information:

[www.alumni.pitt.edu](http://www.alumni.pitt.edu)

### AAMC PITT RECEPTION

NOVEMBER 4

6 p.m.

AAMC Annual Meeting

Marriott Wardman Park Hotel

Washington, D.C.

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Office of the Vice Dean

412-648-9000

[vicedeanstaff@medschool.pitt.edu](mailto:vicedeanstaff@medschool.pitt.edu)

### WINTER ACADEMY

FEBRUARY 22, 2008

Ritz-Carlton

Naples, Fla.

For information or to request

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Pat Carver

412-647-5307

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### WINTER ACADEMY—WEST

MARCH 15, 2008

Arizona Biltmore Resort & Spa

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### MEDICAL ALUMNI

WEEKEND 2008

MAY 16-18, 2008

Reunion Classes:

1948	1953
1958	1963
1968	1973
1978	1983
1988	1993
1998	2003

TO FIND OUT WHAT ELSE IS HAPPENING AT THE MEDICAL SCHOOL, GO TO [www.health.pitt.edu](http://www.health.pitt.edu)



## NOURISH THE YOUNG

While other toddlers counted animal crackers, you toyed with one of those build-a-molecule kits, right? Or perhaps you brandished a toy stethoscope and a reflex hammer that your parents regretted having included in your junior doctor kit. Now that you've realized your dream, another generation awaits your support. Help nurture the development of future generations of medical students. In addition to contributing to your alma mater, you could establish a gift that would provide you (and/or a loved one) with an annual stream of income for life as well as tax advantages. There are many giving opportunities that could benefit both the school and you.

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