UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | NOVEMBER 2004

PITTMED



THE APPLE OF YOUR EYE

HOW FAVORITE TEACHERS THINK



HI HOMESTEAD!

I am one of the players (freshman basketball '58/59) in the photo on page 33 in the August issue ["A Court Jester"]. The three players in the back are Bob Sankey, George Harley, and me. I do not remember the name of the player in the front. Of course, I remember Doc Carlson very well. He was such a delight to be around. As you correctly pointed out in the article, he often called out a person's hometown instead of his name. Numerous times on campus he would spot me and call out, "Hi, Homestead!" He was a real treasure.

J. Charles Anderson (ENGR '63)
Waterford, Mich.

It was orientation week and immature was hardly the word for us—we were apparently disoriented as we were herded to the tiered auditorium to be further oriented.

The ruddy complexion and shock of white hair identified Dr. "Red" Carlson, the men's health director, as he strode to the podium. Then, before launching into a talk on the virtues of masturbation—its sanitary and convenient nature as well as its safety—Carlson told a related and ribald joke. The mixture of loud guffaws and timid giggles separated the sophisticated among us from those of us who were just awestruck.

I was one of those who left high school early in those war years and was part of Carlson's "orientation" early in '43. I thoroughly enjoyed Edwin Kiester's recent portrait of one of Pitt's famous characters. "A Court Jester" is perhaps a first of a very welcome breakthrough for *Pitt Med*; and, unless I'm mistaken, it will be well received by those of us who appreciate the beautiful composition and artwork that goes with each issue of *Pitt Med* but who have learned that there is much more to medicine than that which goes on inside university walls, and much more than clinical and scientific themes.

In short, there is a vast world out there where the bulk of medicine is practiced and where most of us practice. It is a world not only of unusual accomplishment but also of intrigue and politics.

Ralph J. Miller (MD '52)
Indiana, Pa.

Dr. Miller is the author of Doctor in Jeopardy *(Aesculapius Publishing, 1999), which is, as he puts it, "an unvarnished view of the successes and pitfalls of a practice in a community hospital."*

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

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2004 MAGAZINE HONORS

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- Gold Medal, Multipage Design
- Honorable Mention, Magazines
- Honorable Mention, Best Article

Women in Communications
- Matrix Award, Feature Writing
- Honorable Mention, Feature Writing

American Association of Medical Colleges
- Robert G. Fenley Writing Award (for J. Mesman's "Lesotho Diary")

IABC Golden Triangle Awards
- Award of Excellence, Magazine Design (E. Cerri)
- Award of Honor, Magazines
- Award of Honor, Writing (for C. Staresinic's "Dark Winter")

CORRECTIONS/ CLARIFICATIONS

In our last issue, we incorrectly referred to the optic nerve as a pathway for herpes simplex virus infection. The ophthalmic branch of the trigeminal nerve is the pathway followed by the virus.

The Pitt Alumni Signature Series of Continuing Education Lectures presents

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Their recent groundbreaking work has enabled doctors to actually see manifestations of Alzheimer's disease in the brains of living patients.

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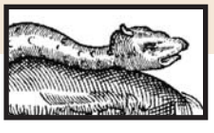
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CONTRIBUTORS

MICHAEL LOTENERO [Cover and "What It Takes to Be a Top Teacher"] sold his first illustration in third grade. He used colored pencils to draw the Star Wars characters R2-D2 and C-3PO on a classmate's notebook. The fee? "Lunch money," says Lotenero. "Probably a buck." About nine years ago, he began illustrating onscreen with a computer mouse, and he now does all of his commercial illustration this way. His fine art paintings have been exhibited from California to New York.

In August, photographer FRANK WALSH ["What Keeps MD/PhDs Humming Through Eight Years of Grad and Med School?"] went to the farm show in Butler County and set up a backdrop in a barn so that he could photograph people at the fair, including children and teens with the sheep, cows, pigs, and chickens they were showing at the event. He was attracted to his subjects' timelessness; the youth didn't wear the latest fashions or shirts with slogans or commercial emblems. Instead, one wore a simple white T-shirt that was dirty from working; another had forgotten his belt and had tied a rope around his waist. A western Pennsylvania native, Walsh studied at the Art Institute of Pittsburgh. His pictures have been described as having "luscious, otherworldly lighting."

COVER

We surveyed top teachers among our faculty and alumni and found that there's a method to their magic. (Cover illustration: © Michael Lotenero. Oath: Hippocrates.)

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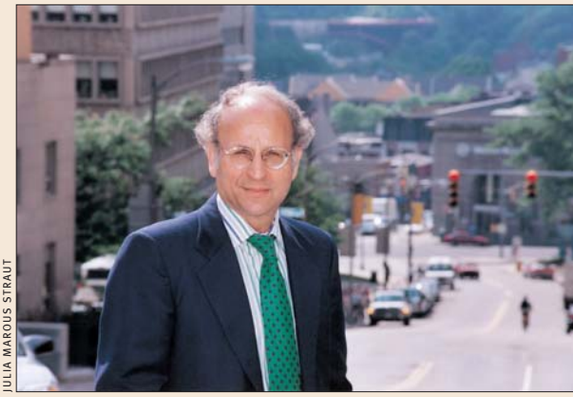
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Pitt Med is published by the Office of the Dean and Senior Vice Chancellor for the Health Sciences in cooperation with the alumni and public affairs offices. It is produced quarterly for alumni, students, staff, faculty, and friends of the School of Medicine. PR 4703

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"If I didn't do it, who else would? There are a lot of people out there younger than me who need to know what [drugs] to take." These words were uttered a couple of years ago by Dorothy, a woman who participated in a clinical trial here for an osteoporosis drug; her participation was covered by this magazine. Dorothy's example makes me think of what Mason Cooley said about generosity—it knows how to count, but refrains. Patients volunteering for clinical trials truly are altruistic and courageous.



JULIA MAROUS STRAUT

Many such trials simply seek to establish the maximum tolerated dose of a new drug when the actual efficacy of that drug is not yet being tested. Other trials have a control arm, in which patients may be randomly assigned to receive the best known treatment for a disease. (Infrequently, the best known treatment may be no treatment, i.e., a placebo.) Patients in the "experimental" arm receive a new treatment that may be better, worse, or the same as the best known treatment. It is easy to understand the reluctance of patients to enroll in a trial. Cultural and social issues also influence such decisions, but whatever the explanation, we need more patient volunteers. The problem is compounded by the changing regulatory climate, notably the advent of HIPAA, which, though well-intentioned in its design to protect patient privacy and confidentiality, has further impeded our ability to recruit volunteers.

For the past several years, many have worried about the future of clinical research in this nation, especially regarding our ability to conduct adequate trials on the safety and efficacy of new drugs. In fact, clinical trials may have to be more extensive and lengthy than in the past—witness the unexpected side effects of Vioxx, detected only after huge numbers of patients had been treated for long periods of time. And while fewer patients are enrolling in clinical trials, fewer young physicians are preparing for careers in clinical research—just when the number of new therapies developed as a consequence of our rapid progress in the laboratory is nothing short of astonishing. I've discussed the dearth of clinician-scientists before on these pages. Among the powerful disincentives to young doctors embarking on this path is a lack of institutional support.

In October, I was invited by Dr. Elias Zerhouni, director of the National Institutes of Health, to spend a day brainstorming with him on innovative approaches for strengthening the nation's clinical research enterprise. Pitt is seen as an exemplar, given our long-term track record in conducting clinical trials. Further, we have a unique Office of Clinical Research that supports and integrates the efforts of all of our health science schools, an approach which is vital in this multidisciplinary and interdisciplinary era; a renowned Center for Clinical Research Education that is focused on preparing students, fellows, and junior faculty; and an Office of Academic Career Development that's concerned with every aspect of developing the next generation of investigators.

What else can academic medicine do to improve the climate for clinical research? As my colleagues consider whether to make institutional changes to address this pressing issue, I ask them again to consider Dorothy's example: If we don't do it, who else will?

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



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EGG DESIGN | ELENA G. CERRI

School Launches New Curriculum

For today's physicians, keeping up with the rapidly growing body of medical literature is no small task. "You have so much that you're faced with reading," says Beth Piraino, professor of medicine. "You have to be able to understand fairly quickly when you look at an article whether the statistics are meaningless, the study design is bad, and you should just discard it, or whether it's something important that you should immediately implement in your practice." Teaching students how to make that distinction is one of the aims of the med school's new Methods and Logic in Medicine course. The underlying goal is to teach students how to continue their education after formal training is over. "What they learn in medical school as far as the nuts and bolts facts, that's going to be out of date so unbelievably fast," says Piraino, one of the codirectors of the course. "If they don't keep up with the literature, they'll just be an outdated doctor very, very quickly."

The course is just one element of the medical school's new curriculum, which is being implemented this fall after an extensive curricular evaluation. One cornerstone of the new curriculum is a "mentored scholarly project," which students will have four years to complete. "Every student will formulate a question about something important in medicine, gather information related to the question, and analyze and interpret the information—with close one-on-one mentoring," says Steven Kanter, vice dean of the medical school. The project, designed to foster independent and creative thinkers, may involve basic science or clinical research. Or it could be less traditional, involving, for example, health policy research, a community-based social science study, or another inquiry that arises from the student's interests.

Another major change: In the past, students weren't able to take electives until the fourth year. In the new curriculum, third-year clerkships will start two months earlier, giving students the option to take electives in the third year and to explore specialized career interests long before the fourth-year residency application process gets under way. "The added flexibility and choice will help students make a solid, durable career decision," says Kanter. *—Dottie Horn*

FOOTNOTE

Since the dawn of civilization, people have been getting drunk. By now, you'd think there'd be a better antidote for a hangover than a raw egg. It was recently reported that extract of prickly pear cactus prevents that "I-can't-even-look-at-food" feeling you might get after imbibing too much. The extract also eases dry mouth. Coincidentally, or perhaps not, the lead author works not far from Bourbon Street in New Orleans.



CAMI MESA

A&Q

With Mark Perlmutter

Shortly after arriving in Thailand, Mark Perlmutter (MD '04) and a friend decided to go to the Royal Palace in downtown Bangkok. They were standing at a bus stop with a map, trying to figure out which bus to take, when a local man offered to help. It turns out they were at the wrong bus stop, but the man took them to the correct stop, waited with them until the bus came, and was going to get on the bus and take them to the palace, which was a two-hour trip away, just to make sure they didn't get lost. (Eventually, Perlmutter convinced the man they'd be able to make it on their own.) Perlmutter says he had similar experiences "at least 10 times" during the year he was in Thailand: "The whole idea of fear of strangers doesn't really exist there. If you're walking down the street, people pull over and ask, 'Do you need a lift?'"

His exposure to Thai culture, especially the people's generosity and concern, has inspired Perlmutter to seek meaningful relationships with patients, "relationships of trust and, hopefully, friendship," he says. The year he spent teaching English in Thailand after college also inspired him to write a book, the ironically titled *A Year Wasted*, which he self-published. "It was one of the best years of my life," says Perlmutter, who recently started a urology residency at New York University.

On differences between American and Thai culture

What [a lot of Thai people] don't have in economic wealth, [many of them] more than make up [for] in interpersonal relations, and I think that's a lot more valuable in many cases than monetary wealth. … I saw the same people on the street in the evenings. The husband and wife would be sitting on the porch with their kids, playing board games or just sitting and chatting. Everybody would be out, sitting together, the kids would be playing together, some of the guys would be talking to their neighbors. … You could see that people were tired after a long day of work, but they were just really enjoying that time together as a family and with their neighbors. And I don't think that we really do that as much here. People just come home and go about their business.

His question for us

All of these things that you experience in your life before medical school really impact you, but how do you hold onto those values you had beforehand in a demanding lifestyle like medicine? *—Interview by Dottie Horn*

SEE PERLMUTTER'S BOOK ONLINE: www.ebookmall.com/ebook/144778-ebook.htm

Faculty Snapshots

Susan Amara, chair of the Department of Neurobiology and a former Howard Hughes Medical Institute investigator, was recently elected to the National Academy of Sciences. Amara's research focuses on neurotransmitter transporters, proteins that take up extra neurotransmitter molecules released from neurons as they communicate with each other in the brain. The transporters play a key role in regulating neurotransmitter levels. She helped discover how cocaine binds to the dopamine transporter and prevents it from functioning, so that extra dopamine builds up between neurons, stimulating the brain's reward system.



Amara

The American Academy of Arts and Sciences recently elected as a fellow **Peter Strick**, a Pitt professor of neurobiology. Founded during the American Revolution, the academy recognizes those who have made exceptional achievements in scholarship, business, the arts, and public affairs. Strick developed a technique to use viruses to trace neuronal circuitry in primates. Not long ago, scientists thought that the cerebellum, a fist-sized structure atop the spinal cord, was involved only in movement, coordination, and balance. Through his primate work and fMRI studies in humans, Strick has shown that the cerebellum is connected to the brain's thinking processes. Strick is codirector of Pitt's new Center for Neuroanatomy with Neurotropic Viruses, for which the University recently received a $4.6 million National Institutes of Health grant. The center will use viruses to trace the circuitry and architecture of the nervous system. Strick also codirects the Center for the Neural Basis of Cognition.



Strick

The National Institutes of Health recently gave **Yan Xu**, professor of anesthesiology, a MERIT (Method to Extend Research in Time) award. The grant will support Xu's work on how general anesthetics work at the molecular level. Through this grant, Xu will have continued support for up to 10 years and will sidestep the usual competitive grant renewal process. **Charles Rinaldo**, professor of pathology with a joint appointment in the Graduate School of Public Health, has also been granted a MERIT award for his work on immunotherapeutic vaccines against HIV. Xu and Rinaldo are the latest among 13 in the School of Medicine given MERIT awards. "With a guaranteed eight to 10 years of funding," says Xu, "you can go into high-risk, high-reward territory." *–DH*



Xu



Rinaldo

SICILIAN TRANSPLANTS

In 1994 and 1995, the Region of Sicily spent $37 million sending Sicilians abroad for liver transplants because there were no facilities that performed the operations in the area. Then the U.S. Congress stipulated that only 5 percent of American organs could go to non-U.S. citizens. Many European countries went further and decided no organs would be allotted to foreigners. Sicilians needing transplants became desperate. Then, in 1997, Sicily partnered with the University of Pittsburgh Medical Center to develop a facility in Palermo, Italy, that would provide transplants and other specialized services. The facility, the Istituto Mediterraneo per i Trapianti e Terapie ad Alta Specializzazione (ISMETT), began operating out of temporary facilities in 1999. Earlier this year, the dream was fully realized—ISMETT opened its new $58 million home, tripling its number of beds and doubling its number of operating rooms. The larger facility will allow ISMETT to expand its living donor transplant program and to provide services not only to southern Italians, but also to more people from other countries in the Mediterranean region. ***—Melanie Donahoo***



Sicily's new transplant hub

Sound Medicine



GETTY

The Frick Room at the Omni William Penn Hotel breaks out in sound, not quite song. The walls echo voices, some high-pitched, some low, as about 150 people choose a random note and hold it. An animated woman at the front of the room has instructed the group to try out a technique: They should begin to "laugh silently" while they continue to produce the sound. The laugh will open up the vocal cords, increasing the distance between them, leading to a more full-bodied sound, she explains, demonstrating with a huge smile and an *aaaaHHAAAA*. She's onto something. As the crowd follows her cue, the sound in the room becomes louder, more voluminous.

This group is participating in a session called "Vocal Physiology and Care of the Choral Voice" during Chorus America, an annual conference for conductors and other choral professionals and aficionados held this year in Pittsburgh. The presenters are Clark Rosen, a Pitt associate professor of otolaryngology who directs the University of Pittsburgh Voice Center, and his staff—including Kimberly Steinhauer, the PhD vocal coach with the silent laugh.

The group has heard Rosen explain how medical conditions, like gastric reflux esophageal disease, can affect the voice. The doctor is just the expert to speak to the group. He created a fellowship program at Pitt to train physicians on how to care for the professional voice. (It's one of only a handful of such programs in the country.) He conducts voice-related research. He's studying, for example, the covering of the vocal cord, which sometimes becomes scarred from screaming, intubation, or trauma to the neck. "The covering is a highly elastic specialized tissue that doesn't exist anyplace else in the body, and so we're learning ways to repair that back to its normal physical properties through tissue engineering," he says. Oh, and did we mention—he's physician for the Pittsburgh Opera. The bulk of his patients are school teachers, attorneys, singers, and others for whom voice health is critical to job performance.

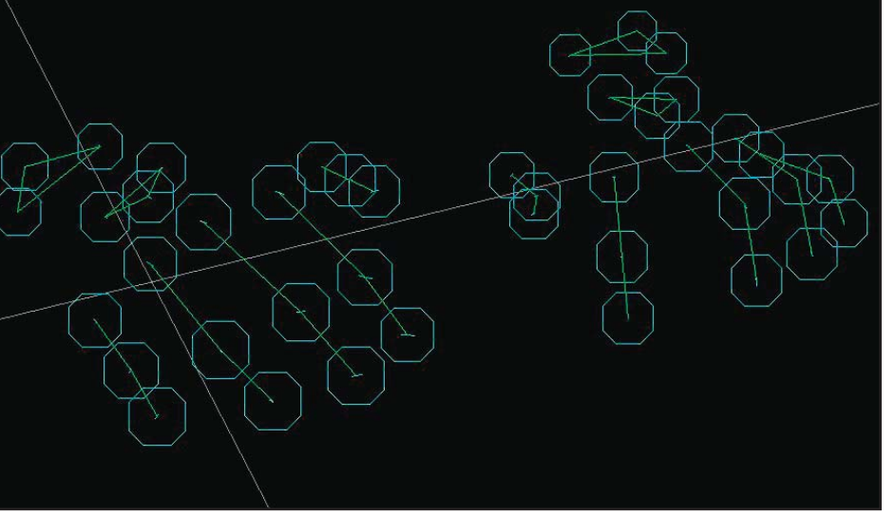
At the end of the session, after taking in Rosen's talk and tips from professionals from the voice center, members of the audience cluster around the presenters, extending their hands, expressing their thanks, eager to learn more. ***—DH***

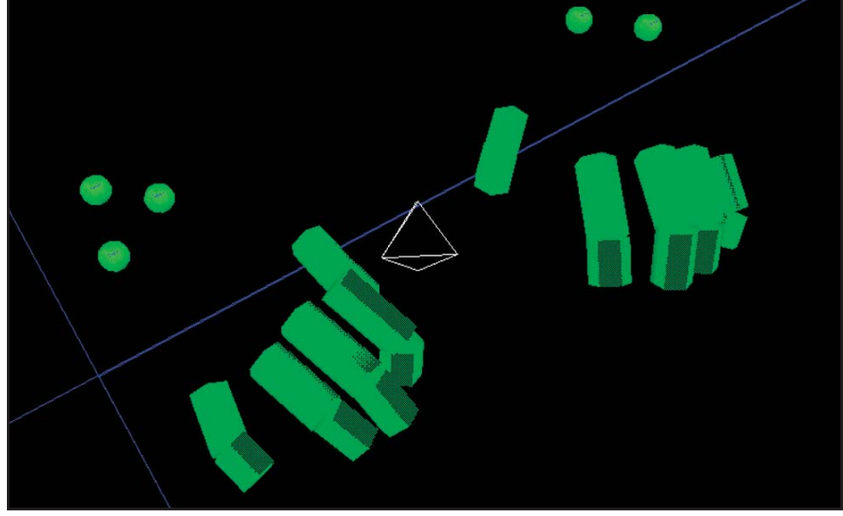
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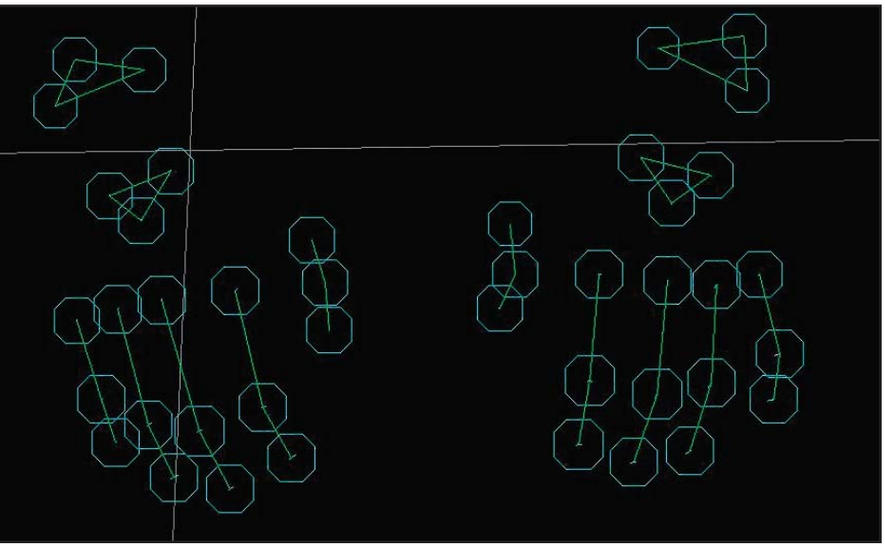
By 2030, one-fifth of the U.S. population will be over 65. Effectively treating the chronic diseases that are prevalent in the elderly will require team-based care, a whole cornucopia of healthcare providers working together to plan and deliver treatment. As the population ages, the incidence of chronic disease is likely to increase, and many believe interprofessional education will be needed to foster a collaborative approach among doctors, pharmacists, physical therapists, dentists, and practitioners in other healthcare fields.

Pitt was recently cited as a model of interprofessional collaboration in geriatrics by the Association of Academic Health Centers (AHC). It was among a handful selected for the recognition out of more than 100 academic health centers; Pitt's strengths included its new graduate-level certificate program in gerontology. All 16 of Pitt's schools, including the law and engineering schools, worked together to create the program, which is open to students in any field.

"It's a major step in the grand scheme of interprofessionalism to be able to get so many different people from so many different schools together to focus on just the issue of geriatrics," says Ryan Mrazik, a program assistant at AHC. *—DH*







COURTESY N. BAKER

FINGERED **Typing never looked so captivating. In Pitt's Human Movement and Balance Laboratory, Nancy Baker, assistant professor of occupational therapy, and Mark Redfern, professor of bioengineering, otolaryngology, and rehabilitation science and technology, capture 3-D motion in videos of typing hands (see stills above) in order to study finger movement patterns associated with carpal tunnel syndrome and other musculoskeletal disorders. The effect is like watching disembodied stick-figure hands type on an unseen keyboard. To create the videos, the researchers place reflective markers on the hands of a study subject. Then, with a technology developed by the Vicon corporation, several cameras placed at various angles track the markers as the person types. A computer records the spatial coordinates of each marker 60 times per second, so that the researchers can quantify the trajectory and speed of each movement. Other researchers have already elucidated problem patterns in wrist movements among typists, which has led to prevention and treatment strategies and dome-shaped ergonomic keyboards. Finger movements during typing, however, remain poorly understood.** ***—Corey Ballantyne***

Appointments

There is no perfect animal model for Parkinson's disease, says **Edward Burton**, an MD/PhD who is a new assistant professor of molecular genetics and biochemistry. In humans, the inherited form of the disease is caused by mutations in the alpha-synuclein gene. (In all forms of human Parkinson's, one characteristic of the disease is the brain's formation of Lewy bodies, which are abnormal clusters of the alpha-synuclein protein.) If you mutate the alpha-synuclein gene in a mouse, however, you get an unexpected result. "The microscopic features [of the mouse brains] don't look like Parkinson's—the wrong cells die," says Burton. At Pitt, Burton plans to develop a zebra fish model of Parkinson's. He hopes the model will help him understand why alpha-synuclein forms Lewy bodies in the neurons of people with Parkinson's, and how the formation of Lewy bodies leads to cell death. Before coming to Pitt, Burton was a clinical lecturer in neurology at Oxford University and a movement disorders physician.



Burton

Cocaine addicts may stop using cocaine, but if they see cocaine-using friends or go back to a place where they used to buy the drug, they sometimes relapse into addiction. Cocaine causes increased levels of the neurotransmitter dopamine in the brain; studies in rats have shown that exposing rats to an environmental cue associated with cocaine availability also triggers a release of dopamine in the brain. The cues trigger craving, researchers thought, because they have a biochemical effect like the drug itself, and cocaine stimulates the desire for more cocaine. But recent research by **Charles Bradberry**, a new associate professor of psychiatry and member of the Center for the Neural Basis of Cognition, shows that in this case, what has been observed in rats does not play out the same in primates. Bradberry found that in monkeys, exposure to environmental cues does not increase dopamine levels, but instead causes a decrease in levels of the neurotransmitter serotonin. His work may lead to drugs that could help former addicts resist temptations set off by environmental cues. Bradberry, a PhD, recently came to Pitt from Yale University.



Bradberry

Fifteen years ago, the technique called nuclear magnetic resonance could be used to determine the three-dimensional shape of only the smallest proteins. Then, **Angela Gronenborn** and her colleagues advanced NMR; now it can be used to define the structure of much larger proteins. Gronenborn has joined the faculty at Pitt; she will direct the newly created program in structural biology. Gronenborn will continue working half-time at the National Institutes of Health until her laboratory at the Biomedical Science Tower 3 is completed in 2005. Gronenborn has used NMR to determine the structure of HIV- and AIDS-related proteins, those of interleukins and cytokines, and some protein complexes involved in transcription regulation. *—DH*



Gronenborn

POWER OF THE PEN

PHYSICIAN-WRITER HELPS SPARK WIDESPREAD CHANGE IN JAPAN

BY KRISTIN OHLSON



COURTESY KUFFNER

Physicians participating in the Pittsburgh-Japan Program faculty development workshop learn about medical simulator education at Pitt's WISER center with Kuffner (in red turtleneck).

As a Brown medical student, Haruko Akatsu Kuffner was startled to hear a pediatrician tell the parents of a baby to make time for themselves amid all the cares of child rearing. "That kind of advice would never be given by a doctor in Japan," Kuffner says. "In Japan, mothers are expected to give 200 percent to their child."

Kuffner wrote down the unexpected advice in her journal. Born and raised in Tokyo, she had dismayed her traditional family by leaving Japan—and the prospect of an arranged marriage followed by motherhood—to go to medical school in the United States at the age of 26.

As a med student, Kuffner was fascinated by her day-to-day experiences and didn't want to forget them. In her journal, she jotted down notes to help jog her memory.

In 1994, right after she finished med school, a publication in Japan asked Kuffner to write a column about what it was like to be trained as a physician in the United States. Her columns were eventually published in two Japanese-language books. The first, *America no Igaku-kyouiku* (*Medical Education in the United States*), published in 1996, focused on her experiences in medical school; the sequel, published in 1999, focused on her residency training.

Kuffner became something of a medical celebrity in Japan. Reform of the Japanese medical education system was a hot topic, and her books rocketed to the top of the charts for books on medical subjects. She was invited to speak at grand rounds and at conferences. Newspapers frequently interviewed her, and she was often asked to write opinion columns.

In Japan, students move directly from high school to six years of medical school. Their med school training is composed almost entirely of lectures. What clinical time they have is usually spent observing physicians, rather than interacting directly with patients. After six years of med school, students take a standardized test. If they pass, they receive a license. Up until recently, they could then begin to practice medicine. Or, if medical school graduates chose to specialize, they selected a mentor, say, an interventional cardiologist. They immediately began to narrowly focus their education without first getting more general clinical training.

After her fellowship, Kuffner returned to Japan and, for two years, worked with the Ministry of Education on medical education reform. Owing in part to her efforts, earlier this year, two years of postgraduate clinical training in general medicine became required for all Japanese medical school graduates.

Kuffner moved back to the United States two years ago to join Pitt's endocrinology division, where she is an assistant professor. At Pitt, she launched the Pittsburgh-Japan Program, which arranges the exchange of both physicians and medical students between UPMC and Japanese medical centers.

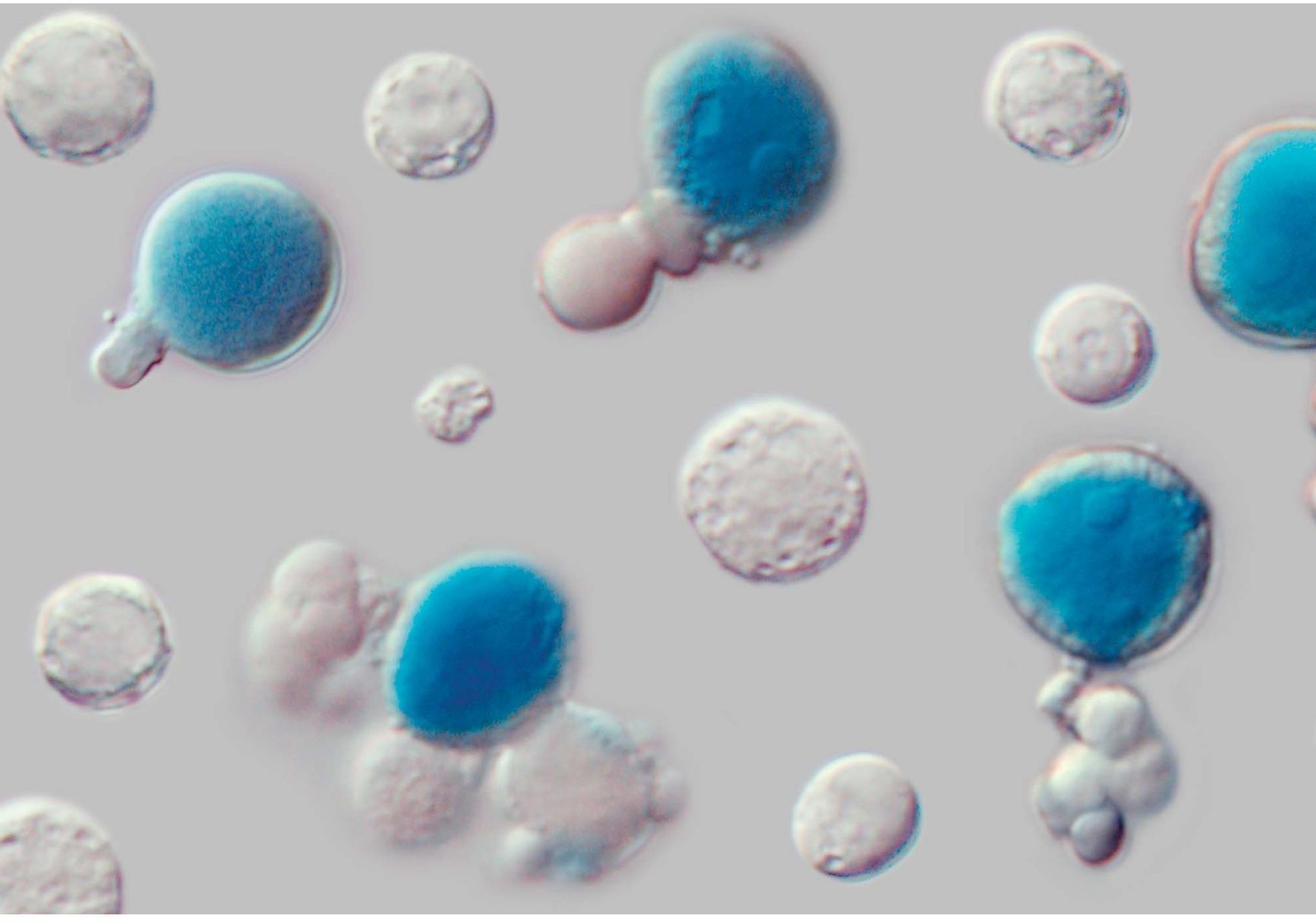
"Internationalization will improve patient care," says Kuffner. "If you're a car manufacturer, pianist, or researcher, you have to compete globally, but when it comes to clinicians, the market has been primarily domestic—clinicians in the U.S. never have to compete against doctors from Japan or France.

"Since clinical medicine is practiced so differently in different countries, we can all learn something from each other."

Kuffner has other books germinating, too. One day she would like to write about being a Japanese professional woman from a very traditional family. She would share, she says,"the choices I made, what I went through, how I felt—so my daughters can read about it." ■

FLASHBACK

It's a familiar story: A man who was 5-foot-5 and weighed more than 200 pounds went on a diet that strictly limited bread, sugar, beer, and potatoes. He ate freely of other foods, however, and lost 35 pounds. The published account of this new diet is widely read and followed. Atkins? Nope, the man's name was Banting, and his diet, known as Bantingism, circa 1892, was described in a Sept. 8, 2004, letter to the editor of the *Journal of the American Medical Association*.



DAMAGED FERTILITY

WHEN STEM CELLS ARE LOST

BY DOTTIE HORN

A 15-year-old boy has cancer. With treatment, he is likely to survive (75 percent of children with cancer are cured), but there is a 7 to 15 percent chance that the treatment will leave him infertile. Because the boy is past puberty, he could provide a semen sample before the

treatment begins. The sperm could be frozen and later used to conceive a child through assisted reproductive technology. But often the treatment must start immediately, within a day or two of the diagnosis, and saving a semen sample means visiting another specialist, which can be logistically complicated. Sometimes, the devastated parents are overwhelmed, unable to think of anything but saving their son's life. Under the stress of facing the disease and the prospect of a difficult treatment regimen, the boy may not even be able to produce a semen sample. Or because of religious or other beliefs, the parents may not want to ask their child to provide one. For any number of reasons, the boy may not give a sample, and his fertility may be lost.

Of course, if a boy has not reached puberty, providing a semen sample is not even a possibility. Currently, there is no option for safeguarding the fertility of prepubescent boys during treatment. However, research by Kyle Orwig, a PhD assistant professor of obstetrics, gynecology, and reproductive sciences, and of molecular genetics and biochemistry, and Stefan Schlatt, a PhD assistant professor of cell biology and physiology, may offer new options to help boys facing cancer, whether they've reached puberty or not. Their research may also help men with cancer, including those facing testicular cancer (the most common cancer in men ages 15 to 40).

Chemotherapy or radiation can kill the stem cells in the testes, and it is these cells that normally give rise to sperm. But what if before the cancer treatment started, the physician was able to take a biopsy from a testicle, a procedure that is not much more complicated than drawing blood, and later use the tissue sample to restore fertility?

Researchers are exploring this strategy. In experiments with mice, they take a testicular biopsy, then manipulate the tissue to derive a solution of cells with a high concentration of sperm-producing (spermatogonial) stem cells. They irradiate the mouse, then put the solution of cells back into its testicle. The mouse becomes fertile again.

Schlatt was the first to use this technique in monkeys—he showed that injection of stem cells enhanced the recovery of the monkey testis following irradiation, though it did not result in normal sperm counts.

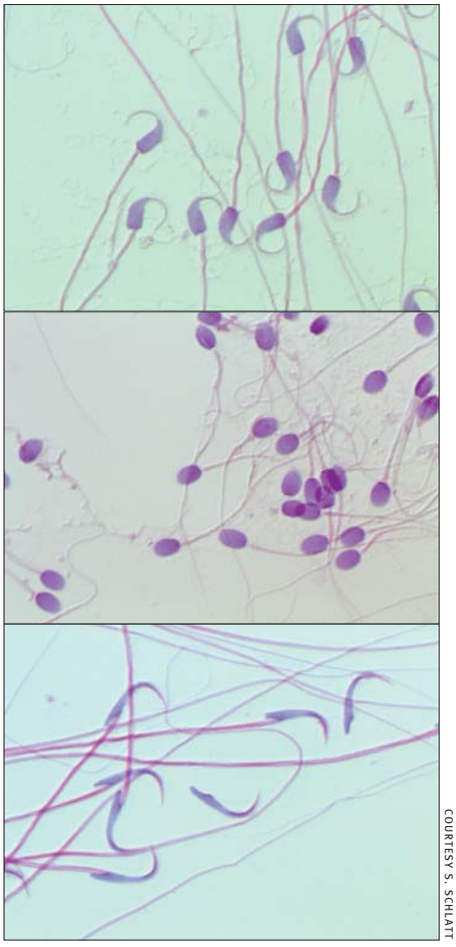
A clinical trial is currently under way in England to study the use of this technique in humans. Seven adult male patients received a transplant of spermatogonial stem cells following cancer treatment. Although Schlatt is not a clinician, he was in the operating room for the first two transplants, guiding the doctors as they performed the procedure.

"The primate testis is quite different from that of mice and other rodents," explains Schlatt. The techniques researchers had developed for performing the transplant in mice did not work in larger animals. Schlatt was the first to show that it was possible to inject the cells into the proper place in the primate testis (by using ultrasound). The expertise Schlatt developed through primate studies was invaluable as the clinicians performed the first transplants in humans.

From each of the study participants, the researchers will take periodic biopsies to compare the testicle that received the stem cell injection to the one that didn't, monitoring their ability to produce sperm.

Although the stem cell transplant technique is promising, it does have risks. "We take cells from a tumorigenic organism. If we put those cells back into the organism, we may be reintroducing cancer," says Schlatt. In one Swedish study, researchers took testicular biopsies from rats with leukemia. Cells from the biopsies were transplanted into the testes of healthy rats who'd been made infertile; they all developed leukemia. The researchers further showed that injecting as few as 20 leukemic cells into the testicle of a healthy rat caused it to develop leukemia. (In the English clinical trial, the patients were selected to minimize the risk of reintroducing their disease—they had cancers that were unlikely to have affected the testes.)

One way to overcome the risk of cancer would be to transplant back into the patient a pure population of stem cells. But how do you ensure that there are no cancer cells mixed in? Orwig has identified rat gonocytes, the primitive embryonic cells that later become sperm-forming adult stem cells. He showed that they have distinctive characteristics, including an arm-like appendage. If such a ready-made marker also exists in adult stem cells, it could



COURTESY S. SCHLATT

OPPOSITE PAGE: Pitt's Kyle Orwig wants to find a way to preserve the fertility of boys and men with cancer. He suggests saving sperm-forming stem cells before radiation and other toxic therapies. But first docs must find those cells. Orwig has discovered that gonocytes in the newborn rat testes have distinctive characteristics, including a large arm-like appendage, which allows them to be distinguished from other cells. Gonocytes turn into sperm-forming stem cells. In the gonocytes pictured here, the nucleus is stained blue (the nucleus is so large it fills up nearly the entire cell). As a gonocyte develops into a stem cell, it loses the appendage. Orwig is now looking for distinguishing characteristics that would enable him to pick out these stem cells in older rats. ABOVE, FROM TOP: Sperm from a hamster, monkey, and rat. In another study, Stefan Schlatt has been able to grow all three types of sperm in the back of a mouse.

COURTESY K. ORWIG

help researchers create cancer-cell free populations of stem cells.

Because of the problems associated with the transplantation technique, Schlatt is also pursuing an alternative approach. A few years ago, he took a testicular biopsy from a pig. He placed a small piece of the testicular tissue underneath the skin on the back of a mouse. (The mouse had been bred not to reject tissue from other species.) Inside the mouse, new blood vessels grew into the tissue, nourishing it with mouse blood. The testicular tissue eventually formed normal pig sperm. His paper describing the success of this technique in generating mouse, pig, and goat sperm was published in *Nature* in 2002. He has since used the same process to generate monkey sperm.

Schlatt has also performed studies implanting human testicular tissue into the backs of mice. The tissue was obtained from male-to-female transsexual patients who had their testes removed. While the tissue survived in the mouse, it never produced sperm—because, Schlatt believes, the patients had received treatment with estrogen prior to surgery, and estrogen badly damages the testes. In the next year, Schlatt and Orwig will do the same experiment with human tissue that has not been compromised by estrogen.

By using the mouse as a "bioincubator" for generating sperm, doctors would avoid any possibility of reintroducing cancer into a patient, but the technique raises other concerns. For example, a virus from the animal could move into the sperm.

Although his studies are preclinical, Schlatt believes they show enough promise that physicians should take action now. "I believe we should ask doctors to freeze tissue, whenever it is available, to keep these possible options open," he says.



C.E. MITCHELL

Three Hampton College students spent their summers at UPCI: (from left) Dakisha Felder, Nikkia Sawyer, and Crystal Woodard.

SUMMER EXPOSURE

UPCI PROF BUILDS LINKS WITH HISTORICALLY BLACK COLLEGE

BY LOIS BARON

Cancer mortality among Blacks is nearly 10 percent higher than in Whites, yet African American cancer researchers are rare. Richard Steinman, an MD/PhD assistant professor of medicine and pharmacology, wanted to do something to increase the number of African American scientists. So Steinman approached Hampton University, in Virginia, which has among the highest number of biology majors of any historically Black college or university. Together with Cecile Andraos-Selim, an associate professor of biology at Hampton, Steinman obtained a $750,000 National Cancer Institute grant. They forged a plan for making Hampton's biology curriculum more lab based. They wanted to improve students' chances of getting into medical or graduate school and encourage them to consider careers in cancer research.

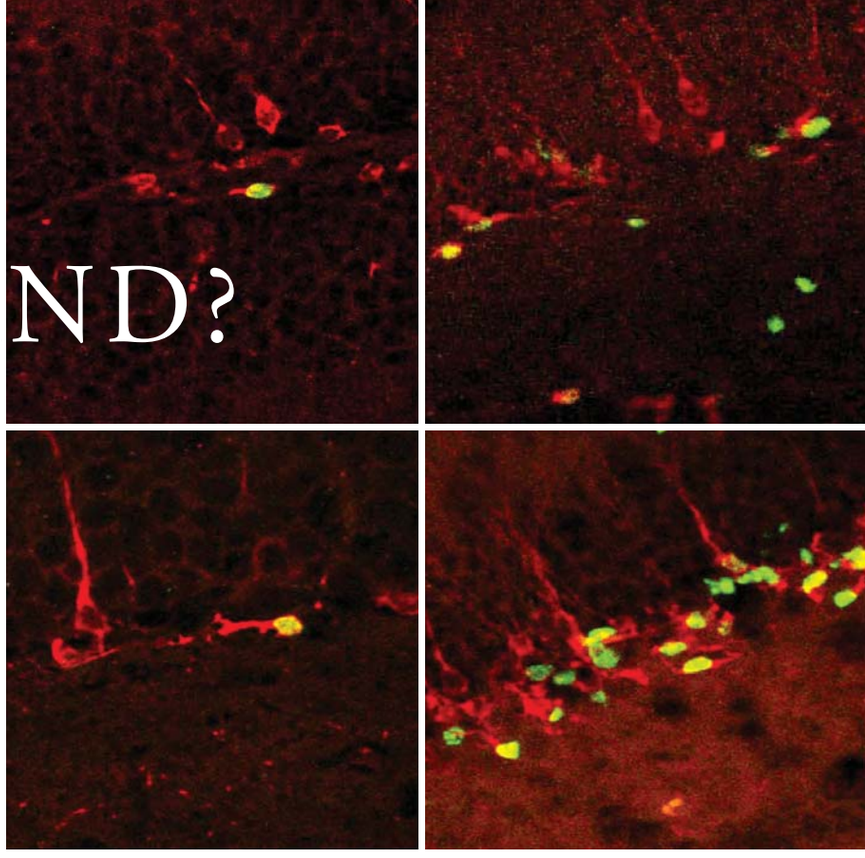
As part of the program, which started last year, three Hampton students spent 10 weeks at the University of Pittsburgh Cancer Institute this summer. For Dakisha Felder, a 21-year-old biology major from Detroit, it was the first time she'd ever helped staff a lab. She'd taken Hampton's new Cancer Biology course. (Steinman helped develop the curriculum for the course and taught some of the lectures on the Web and through videoconferencing.) Before coming to work in Steinman's lab, Felder thought she'd be given a protocol to follow—*Do this, do that.* "It was 100 percent better than that," she says. She found that Steinman encouraged her to think of experiments she could do to answer her questions and let her know that her work was vital to the efforts of the lab.

While in Pittsburgh, Felder presented her work weekly, took part in an ethics forum, interviewed a cancer survivor, shadowed an otolaryngologist, got advice on interviewing for medical and graduate school—she also went whitewater rafting with the two other Hampton students. Now a senior, Felder is applying to MD/PhD programs. "This program sealed it for me," she says. "I want to be a physician-scientist."

STEM CELLS ON DEMAND?

WE'RE CLOSE NOW, AND THAT'S A BOON TO LEUKEMIA RESEARCH

BY ERICA LLOYD



Adult stem cells proliferating on demand: The lower right image shows increased cell progeny after deleting a key cell-cycle molecule (p21) in neurons.

As a medical student, Tao Cheng shared a dorm room with seven others from Shanghai Second Military Medical University. His bunkmate was Bin Zhong Hui, a young man who loved to read and sing traditional songs. By their second year in school, Hui and Cheng had become close. One late afternoon, they'd returned from playing a game of soccer, and Hui told Cheng he wasn't feeling well. His body temperature had spiked, so Cheng went with him to the emergency room. A half hour later, the diagnosis came: Leukemia. A month later, Cheng's good friend was dead. This was the first time Cheng "so deeply felt the great danger of such a blood cancer," he says.

Cheng knew he wanted to be a hematologist before he even took his general medicine rotation. And as a doctor in Shanghai, he saw the same story play out again and again. Leukemia patients died all the time at the hospital. It came to the point where he couldn't bear to be in the clinic; he knew there was work to be done in the lab if doctors could ever hope to save significantly more lives. Today, Cheng is director of stem cell biology research at the University of Pittsburgh Cancer Institute. Building on work he started at Harvard University, he has identified how adult stem cells are activated and maintained. Such findings are likely to increase the odds that future patients diagnosed with leukemia, lymphoma, and other diseases can be treated with stem cell transplants.

An effective treatment for leukemia is a bone marrow transplant. This involves enduring chemotherapy or radiation treatment to kill cancerous cells in the blood. Then, blood-forming adult stem cells that have been removed from the bone marrow of a donor are given to the patient, proliferating and restoring the body's blood cells. A transplant is considered if a patient is fortunate enough to have found a donor with key antigens that complement his or her own, what's known as an HLA match. Patients are most likely to find a match from a close relative. If that's unsuccessful, as it is for about 60 to 70 percent of patients, they can try to find an unrelated donor.

More than 70 diseases are treatable by transplanting blood-forming stem cells, yet there aren't enough donors to go around. The National Marrow Donor Program reports that 8,000 people are formally searching for an HLA donor match in the national registry at any given time, yet only about 16,000 people worldwide have secured transplants through the registry since its inception in 1987. David Scadden, Cheng's collaborator and former adviser at Harvard, estimates there aren't enough stem cells available for a third of all people needing donations.

"There's no worse setting than to tell a patient that you have the ability to cure this disease but don't have enough cells," says Scadden.

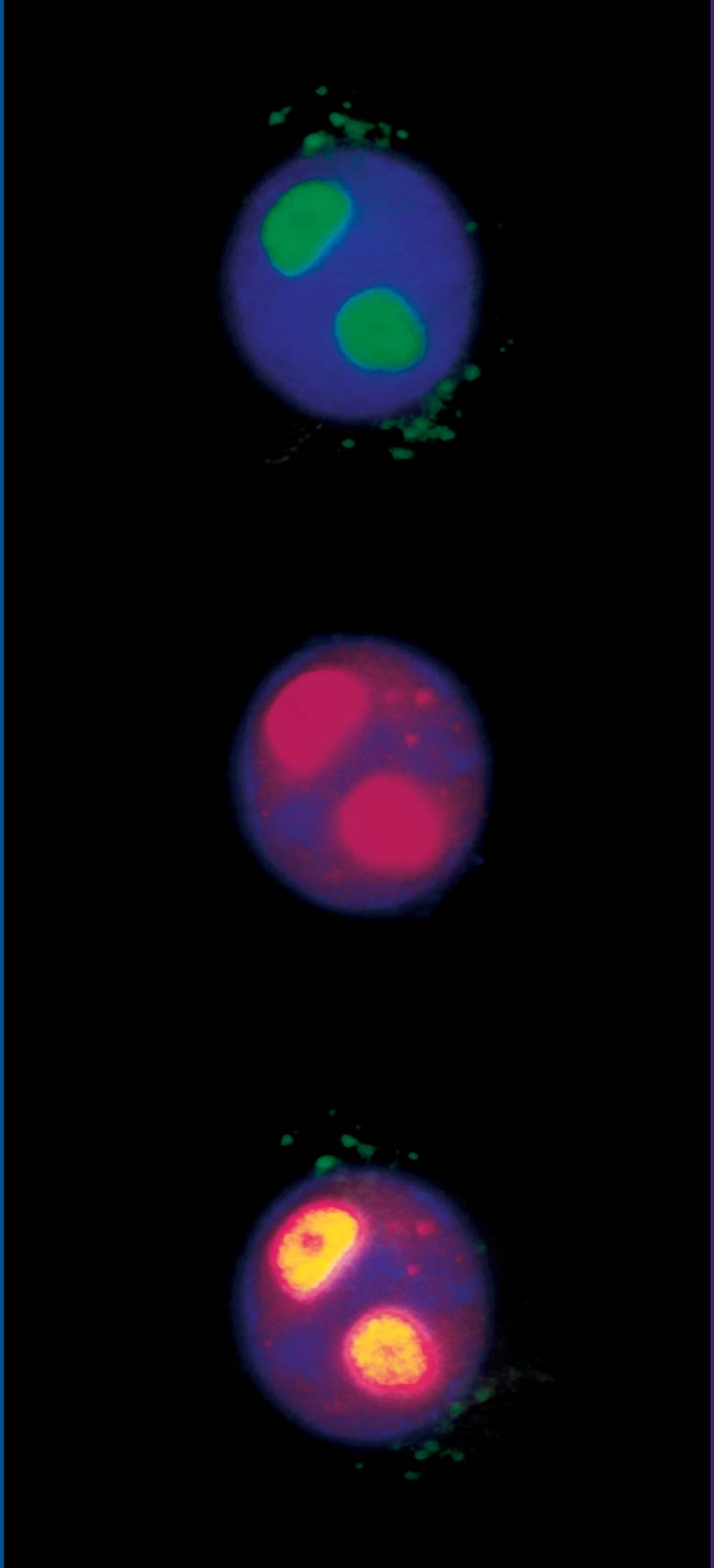
Adult stem cells repair and maintain tissue and organs as needed. But as we age, they start to take it easy. Scientists would love to "wake them up" on demand when the body is in decay or when its repair system has shut down. They've imagined a role for awakened adult stem cells for every part of the body: more blood cells for leukemia and lymphoma patients, more neurons to cure Parkinson's, more cartilage to cure arthritis… But how do we get enough healthy stem cells to keep up with the imagination?

Funding Tao Cheng seems like a good step in this direction. Cheng has identified molecules that regulate key mechanisms of the stem cell cycle. By targeting a molecule known as p21, which normally inhibits replication, Cheng is able to "wake up" blood-forming stem cells so they'll proliferate in knockout mice. But afterward, the stem cells become exhausted and can no longer do their job. Inhibiting another molecule, p18, doesn't seem to affect the rate of the cycle but keeps the stem cells healthy after replication. And when Cheng deletes a molecule known as p27 from the cell cycle, stem cell progeny are increased. The stem cell becomes more efficient.

Cheng suspects he'll find the family of molecules he has identified will work similarly in other adult stem cells as well. They do in stem cells that build neurons.

He envisions therapies for leukemia and other diseases: Doctors would temporarily shut down these molecules until the patient has a healthy and sufficient stable of stem cells. Cheng is now silencing the expression of p18 in human stem cells that have been placed in immunodeficient mice. The success of such a study would be noteworthy. It would be a persuasive piece of testimony to present FDA officials one day, to allow investigators to pursue clinical trials. ■

IMAGE REPRODUCED FROM THE JOURNAL OF EXPERIMENTAL MEDICINE, 1997, VOL. 199, P. 941, BY COPYRIGHT PERMISSION OF THE ROCKEFELLER UNIVERSITY PRESS.



A misfolded protein can be devastating. In diseases as broad ranging as Huntington's, breast cancer, and cystic fibrosis, researchers are considering a new tactic: employing molecular chaperones.

RIGHT: Like firefighters called out to quench a raging blaze, molecular chaperones known as heat shock proteins (HSPs) respond to cellular stress. One type of HSP is trying to help the damaged cell shown three times here. The stress responding HSP (top) is found in exactly the same place in the cell as the abnormal clumps, or aggregates, of misshapen protein (middle), which are associated with disease. In the bottom image, the top and middle images are digitally overlaid, demonstrating the overlap of the HSP and the aggregates.

DOES HUNTINGTON'S DISEASE NEED CHAPERONES? | BY DOTTIE HORN

WHEN PROTEINS CAN'T GET IT RIGHT

Ron Bailey wasn't sure what was wrong. A few years earlier, he'd been laid off from his position as an account executive, where he'd earned, with bonuses, about $75,000 a year. Since then, he'd taken whatever work he could find, mostly odd jobs. He was in his mid-40s and the primary breadwinner of his family. His wife worked part-time; together, they supported two children. But eventually, Bailey found that he just couldn't stay employed. Each new job might last a few months or a few days. He trained as a cashier at one store but could not ring up the merchandise fast enough. He worked in the collections department at another but was too slow on the computer.

Money was becoming tight. Two family cars were repossessed. Bailey and his wife couldn't make the mortgage payments on the house they'd owned for more than a decade. Nor could they pay the back taxes they owed on the house. The sheriff made plans to sell the house in order to pay off the delinquent obligations. By filing for bankruptcy, Bailey saved the house.

COURTESY NATURE PUBLISHING GROUP

Then, Bailey got a job working in a food warehouse, where he loaded trucks using a forklift and made deliveries.

The job was going well, though several times at the warehouse, Bailey lost his balance and fell. One day, after he had been at the warehouse for about six months, he was working on top of an enormous cooler and fell again. This time, he dropped 50 feet and hit his head on a cement floor. Amazingly, he didn't break any bones and wasn't injured by the fall. But once he got up off the floor, he went straight to his supervisor and quit. This was the worst fall he'd had. He felt it wasn't safe for him to work there anymore.

Family members convinced him to see a neurologist. They thought maybe he'd had a concussion or a stroke. The doctor asked Bailey to count down from 100 in increments of seven. Bailey got to 93 and couldn't continue. Then, the neurologist asked him to start with George W. Bush and go backward, naming the preceding U.S. presidents in order. Bailey had always been, he says, "a big freak" about the presidents—he could name them all. By then, he could name only the last four.

The neurologist had a devastating, though still tentative, diagnosis: He was fairly sure that Bailey had Huntington's disease, a fatal, progressive neurodegenerative disease. The neurologist sent Bailey's blood away for genetic testing. Bailey had to wait three months to find out that he had the disease.

During the months of waiting, Bailey had done some research—so he knew the destruction the disease wreaks. Huntington's patients develop involuntary, fleeting, jerking movements, which can affect the hands, feet, face, head, limbs, and trunk. Due to loss of motor control, people with the disease become less able to walk, speak, and swallow. As Huntington's progresses, short-term memory and the ability to concentrate become worse; the patient eventually develops dementia. Huntington's patients also experience emotional symptoms, such as uninhibited behavior. A person with Huntington's typically dies from the disease about 15 years after the onset of symptoms.

After the diagnosis, it took Bailey a couple of months before he was able to adopt a positive attitude. "There is going to come a time when I'm not going to be able to take care of myself," he says, "but I try not to think about it. I try to live each minute I can, do what I can, but it is tough."

Bailey's home was put up for sheriff's sale again. This time, because he knew that he had a disabling illness, he was able to get the mortgage payments reduced. His wife took a full-time job, and he started receiving a monthly Social Security disability check. But Bailey is not yet eligible for Medicare, and his wife's job provides no health insurance, so right now, the family is paying Bailey's medical expenses.

A year after his diagnosis, 48-year-old Bailey is doing everything he can to slow the progression of the disease. He takes vitamins his doctor recommended and minocycline, an antibiotic, which has been shown to protect the brain against Huntington's and other diseases resulting in dementia. Minocycline is believed to increase the life expectancy of Huntington's patients by a few years. Staying active can diminish the disease's impact, so every day, Bailey lifts 10-pound weights and walks three miles. He hates not working and gets bored during the days, while his wife is at work and his kids are at school, but he stays busy playing the drums, calling friends, doing laundry, washing dishes, mowing the lawn.

"I'm so excited every morning," he says. "I wake up and thank God that we kept the house, and [I'm] just trying to take good care of it now."

The toughest thing, he says, is not knowing "what's going to happen down the road, what type of nursing home I'm going to be in, how tough it's going to be on me and my wife." He worries about his kids; he knows each of his children have a 50 percent chance of ending up with the disease. He takes comfort in the fact that the disease progresses slowly. But late at night, he sometimes cries. "That's when my wife cries, too. [It's] the only time the kids aren't around," he says.

All the devastation caused by Bailey's disease results from a certain protein that is too long and has the wrong shape. Inside a cell, as a protein is made, it emerges as a long straight row of linked amino acids. The chain can be as short as a dozen amino acids or as long as several thousand. As soon as it's complete, the linear string then folds into a three-dimensional shape, with loops and curves and helices and crests and pockets. For each protein, there is only one correct way for it to fold, and it can only do the job it was created to do if it folds correctly.

But folding is no easy task. It's so problematic, that for some kinds of proteins, 60 to 80 percent of the protein that's produced folds incorrectly and has to be destroyed. Overall, perhaps a third of the proteins our bodies make don't fold correctly and are summarily done away with. It seems an awful waste of energy—to make all that protein only to destroy it. But to the cell, it's better than the alternative of leaving a misfolded protein in its midst.

If not destroyed, misfolded proteins tend to lump together into globs known as aggregates, which often are associated with disease.

These aggregates are a hallmark of Huntington's disease. In Huntington's, a genetic mutation causes the huntingtin protein to misform. (The protein is spelled differently than the disease.) Normally, in the midst of this protein's amino acid string, there is a point at which the amino acid glutamine is repeated up to 26 times (there is individual variability in the number of glutamine repeats). In people with the disease, however, there are one or more extra glutamines—so that instead of, say, 25 glutamines, there can be anywhere between 27 and 130 glutamines in a row. The extra glutamines cause the protein to misfold, and the misshapen protein lumps into aggregates. In Huntington's, these clumps are found in cells in certain regions of the brain.

But the cell has a natural quality-control mechanism to guard against the ill consequences of misfolded proteins. This is why a third of all proteins are destroyed almost as soon as they are made. "A cell has a choice—to exhibit caution and risk cell death or to shoot first and ask questions later," says Jeffrey Brodsky, associate professor of biological sciences. "We have a hyperactive protein quality-control system that shoots anyone it suspects of being a troublemaker."

One prime feature of the quality-control system: the proteins called molecular chaperones. The first thing seen by a newly made protein are chaperones, notes Brodsky: "They're the first helpers." The chaperone assists the protein in its efforts to fold and is likely to give the protein several chances to fold correctly—but if it doesn't, the chaperone is quick to step out of its nurturing role. It will become a stern judge, condemning the protein—which can't quite master the correct conformation of loops and curves and spirals—to destruction. (Some chaperones are either helpers or judges; others play both roles.) The chaperone looks out for the overall well-being of the cell.

But in Huntington's, the quality-control system somehow fails to rid the cell of all the misfolded huntingtin protein. Brodsky, along with Donald DeFranco, professor of pharmacology and neuroscience, wonders if chaperones might become part of a treatment strategy for the disease. If researchers could manipulate the

"We have a hyperactive protein quality-control system that shoots anyone it suspects of being a troublemaker."

cell so that it had more chaperones, would those extra sentinels be able to get rid of more of the mutated and misfolded protein, before it formed aggregates? Could chaperones someday be used to help people like Ron Bailey stave off the debilitating effects of Huntington's?

DeFranco, a fast-talking, dark-haired PhD originally from New Haven, Conn., decided to test this idea. He contacted a group of scientists at Baylor College of Medicine and arranged a collaboration. The researchers chose to use spinocerebellar ataxia as a model for Huntington's. Huntington's is one of a family of polyglutamine diseases that are caused by excessive glutamine repeats. Like all the polyglutamine diseases, spinocerebellar ataxia is a fatal genetic neurodegenerative disease; it affects coordination and leads to unsteady walking and difficulties in swallowing. The collaborators chose spinocerebellar ataxia because, at the time, it was easier to study than Huntington's—but the results would be generalizable to all polyglutamine diseases.

First, DeFranco inserted into human cells the mutated gene for ataxin-1, the protein that has excessive glutamines in spinocerebellar ataxia. Later, he looked into the microscope. Aggregates of the mutated ataxin-1 protein had formed in the cells. Next, he looked to see where in the cells the heat shock proteins (HSPs) were. (HSPs are one kind of molecular chaperone.) DeFranco's team discovered that the HSPs, which are normally dispersed throughout the cell, had congregated at the site of the aggregates. DeFranco suspected the HSPs were doing something to try to fix what was going wrong.

As a further test, the researchers genetically manipulated the cells so that they would produce more (overexpress) HSP. The cells with more HSP had fewer aggregates.

DeFranco described these studies in an influential paper published in *Nature Genetics* in 1998; it was the first time anyone had linked molecular chaperones to polyglutamine diseases. "There's very likely to be a protective effect against brain injury if we can somehow boost up heat shock proteins," says DeFranco.

If you subject cells growing in culture to the stress of heat, the amount of heat shock protein increases—hence the name. Researchers discovered that HSP defends the cell against temperatures that are too high as well as other kinds of stress. HSP levels increase when the cell is under duress from, say, insufficient oxygen or an acute injury. It's even been found that when mice are restrained in order to induce psychological stress, some of their cells start to produce more HSP.

Because HSP is part of the cell's response to stress, researchers suspect that manipulating HSP levels could be useful in treating many different diseases. Scientists have shown that increasing HSP has a neuroprotective effect in a fly model of Parkinson's disease. A clinical trial is currently under way to test an HSP-affecting drug against breast cancer. In a cat model, DeFranco studies whether increasing HSP might be effective in reducing brain injury from stroke. HSP manipulation has also been considered as a way to treat Alzheimer's disease and cystic fibrosis.

Since DeFranco's pivotal paper linking HSPs to polyglutamine diseases, he and others have searched for a compound that might be used to treat these diseases. They have zeroed in on the compound geldanamycin and its variants. When administered to cells growing in a dish, geldanamycin increases HSP levels. But can it repair an injured brain? One group in Cincinnati injected the compound directly into the brains of rats modeling human stroke and observed some recovery. But in a similar study in rats modeling brain injury from cardiac arrest, DeFranco and Clifton Callaway, Pitt associate professor of emergency medicine, observed no recovery. The effectiveness of geldanamycin in animal models is spotty, and there are other hurdles to overcome. The geldanamycin compounds don't cross the blood-brain barrier—so unless injected into the brain (not a practical treatment strategy for people), they never reach the brain cells where the aggregates form.

DeFranco is collaborating with a California company to test derivatives of geldanamycin to see if these new compounds will cross the blood-brain barrier. He injects the compounds into rats and then looks at their brains a few days later, checking to see if the compound reached the brain. So far, the answer has been no. The problem seems to be intractable.

"Since the mid-to-late-'90s, there have been compounds that people realized were effective agents to induce HSPs, but some eight years later, we still don't have a compound that crosses the blood-brain barrier," says DeFranco.

Even if the researchers can conquer the barrier problem, another issue remains. HSPs are found in every tissue in the body. If researchers find a compound that will increase HSP levels in the brain, to what extent will it affect other tissues in the body, having extensive and possibly deleterious results?

"Eight or 10 years ago, a number of companies gave up on these HSP-binding drugs, because they thought, 'Every cell has heat shock proteins. There's no way that we're going to be able to develop drugs that are useful and that are not going to have side effects everywhere,'" says DeFranco.

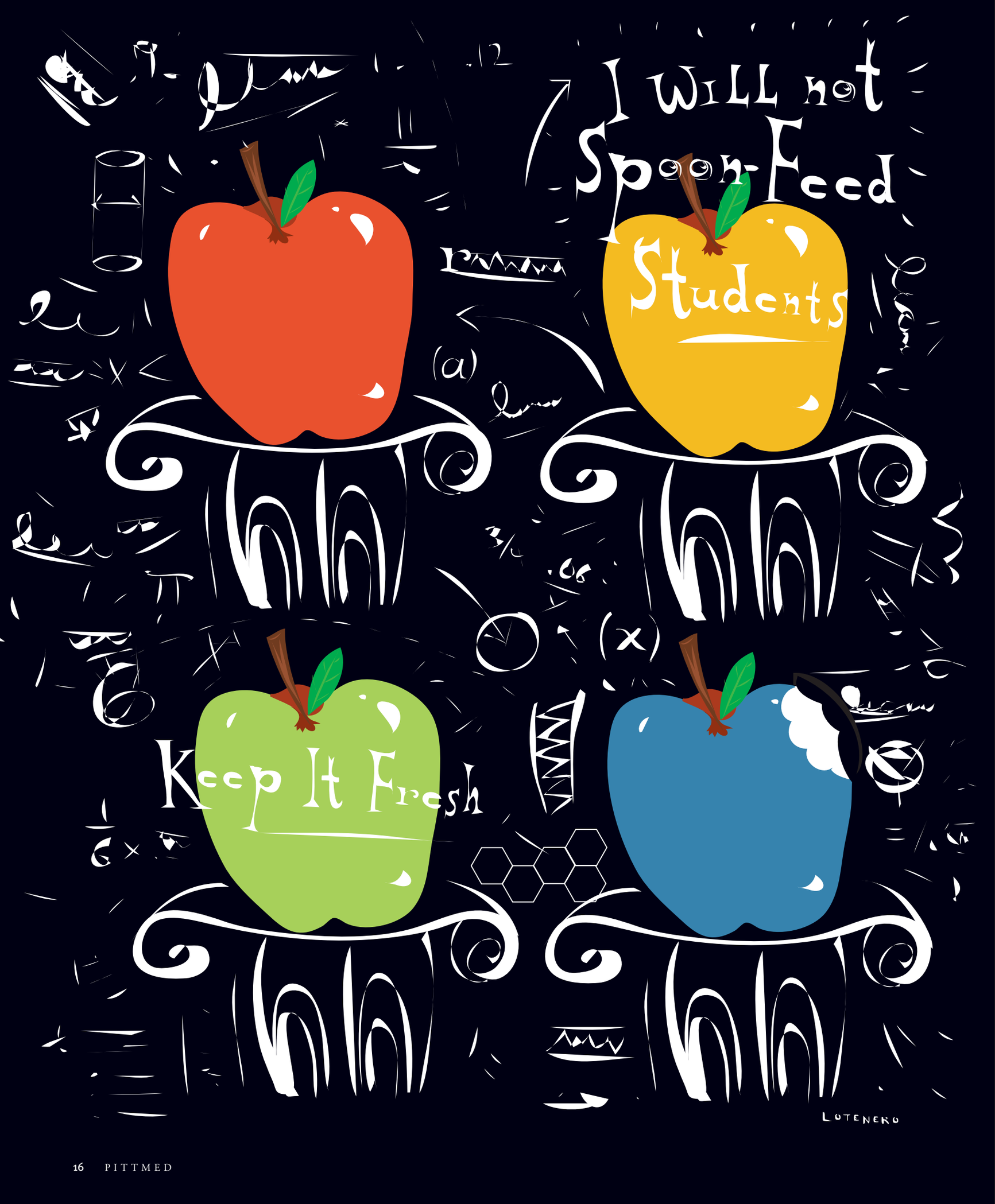
But the pharmaceutical industry has perhaps been encouraged by its success in developing selective estrogen receptor modulators (SERMs). Estrogen acts on many tissues in the body; manipulating estrogen to achieve a desired effect in one tissue can lead to adverse effects in others. But with a SERM, a single drug has different effects in different tissues—enhancing the action of estrogen in some tissues, blocking estrogen action elsewhere. "There's a new way of thinking in the pharmaceutical industry, as far as I can see, that we shouldn't ignore these diffuse targets," says DeFranco.

Ask DeFranco what the chances are that we'll get an HSP-inducing drug that will help the brain, and he sighs. "You know, it seems like it really should happen," he says. He cites two studies in which researchers genetically manipulated mice to overexpress HSP 70, a type of heat shock protein. "And I always thought that would be crazy, to try to overexpress HSP 70 all over, in all mouse tissues, and have the animal still survive and still function," says DeFranco. But, in fact, the mice seemed able to tolerate the extra amounts of HSP 70—and the protein *did* help protect their brains against polyglutamine disease.

Still, the mice were followed for only a short time—whereas a chronic disease like Huntington's would likely require long-term treatment. "How long [would] you try to maintain hyperactivation of heat shock protein?" wonders DeFranco. It might be more feasible to use HSP inducers in acute situations, like stroke.

"Managing chronic neurodegenerative diseases, that's going to be a tough one," he says, "but worth the effort." ■

For privacy reasons, the patient's name was changed in this story.


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AWARD-WINNING PROFS FESS UP

COMPILED BY MEGHAN HOLOHAN, ERICA LLOYD, JESSICA MESMAN, AND JONATHAN SZISH

WHAT IT TAKES TO BE A TOP TEACHER

You know the ones we're talking about. The people who excite us about the life of the mind. Who won't let us get away with bluffing. Who make us aspire to be the very best we can be. Whose simple actions touch a sense of truth in us about what it means to live skillfully. Who aren't afraid to unplug a PowerPoint presentation.

We may not have even appreciated them until years later, but they are our favorite teachers. These creatures whose influence is so profound, how do they make it happen? To find out, we knocked on doors and filled e-mail boxes belonging to award-winning profs among our faculty and alumni. (A list of these sages is on p. 18.) These pages give us a glimpse of how they think, what makes them effective, and who colored their worlds.

ILLUSTRATIONS | MICHAEL LOTENERO



Tried and True

Guidance from the experts.

"You can't just give bare facts," says Basil Zitelli. "You have to tell how or why something occurs so students understand it."

Trust students to learn information on their own, so they're empowered, offers Gerald Merenstein.

Review the basics before moving on, no matter the level of the audience. "Otherwise, you're building a house on a shaky foundation," says Jamie Johnston.

Put as much time into planning the progression of your lectures as you do getting the talking points down on paper, suggests Cynthia Lance-Jones. She stresses the importance of linking ideas in a logical progression.

You have to know your audience, say Zitelli and Johnston, so you know the level you're pitching to. Often, physicians give lectures at a higher level of experience or education than is appropriate.

More than five basic ideas in a lecture are too many, says Johnston: "Some teachers just spray knowledge at you like a fire hydrant; you try to take a sip, and you get your lips ripped off."

Find ways to make the material fresh, even for yourself, says Johnston. One way to maintain enthusiasm when you're covering a topic for the hundredth time, he offers, is to remind yourself of the significance of your job. "Teaching is often not as sexy as surgery," he says. "But I'm helping a new generation of doctors whose patients will be affected by what I do in the classroom. And I can always get enthusiastic about patient care. That's why I do what I do."

Constructive criticism is vital, says Paul Rogers. At the same time, Rogers recommends telling students up front that they're going to get a lot of feedback so they realize it's part of the process and not a reflection on their performance. Adjust your teaching methods to meet student needs. "Give more or less feedback, more detailed instruction, change your curriculum, whatever it takes," he says.

Make students evaluate themselves. Heidi Feldman uses this tool so her students can learn their strengths and weaknesses and so that she can work on her listening skills.

Use different teaching formats, advises Carole Coffee. While she appreciates the value of the lecture, she is glad that there is a movement toward more problem-based approaches. "It's important to have a curriculum where the students have room to teach each other and themselves."

Remember that a professor can't teach everything that a student needs to know, says Gerald Merenstein. ■

Thanks to these sage teachers among our faculty and alumni, whom we canvassed for this feature:

Carole Coffee, professor emeritus of molecular genetics and biochemistry at Pitt, winner of the Chancellor's Distinguished Teaching Award

Georgia Duker (PhD '82), assistant professor of cell biology and physiology at Pitt, winner of the Chancellor's Distinguished Teaching Award, the Golden Apple, and six-time recipient of the Excellence in Education Award

Heidi Feldman, Ronald L. and Patricia M. Violi Professor of Child Development and Pediatrics at Pitt, winner of the Chancellor's Distinguished Teaching Award

Jamie Johnston (MD '79), professor of medicine at Pitt and a recipient of the Chancellor's Distinguished Teaching Award, Excellence in Education Award (six times), Pitt's Golden Apple, the National Golden Apple, and an Unsung Hero Award for outstanding resident teaching at West Penn Hospital

Cynthia Lance-Jones, associate professor of neurobiology at Pitt and a recipient of Pitt's Excellence in Education Award and

...es

the Kenneth E. Schuit Award, Dean's Award for Master Educator

Gerald Merenstein (MD '66), professor of pediatrics at the University of Colorado, two-time winner of the Outstanding Teacher Award, Department of Pediatrics, Fitzsimons Army Medical Center

Joel Merenstein (MD '60, Res '61), clinical professor of family medicine and director of research and fellowships at UPMC St. Margaret; winner of the Society of Teachers of Family Medicine Excellence in Education Award

R. Harsha Rao (Fel '88), professor of medicine, director of fellowship training in Pitt's Division of Endocrinology, recipient of the Chancellor's Distinguished Teaching Award

Paul Rogers, professor of critical care medicine and medicine at Pitt and a five-time recipient of the Golden Apple, winner of the Chancellor's Distinguished Teaching Award, the Kenneth Schuit Award, and the Leonard Tow Humanism in Medicine Award

Nina Schor, assistant dean for medical student research at Pitt and professor of pediatrics, neurology, and pharmacology; recipient of the Chancellor's Distinguished Teaching Award

Basil Zitelli (MD '71), Pitt professor of pediatrics and recipient of the Kenneth Schuit Award

Things Fall Apart

Do great teachers ever make mistakes? Yup. Top faculty reported failed projector bulbs and then some.

Nearly 25 years ago, Joel Merenstein was teaching residents at what is now UPMC St. Margaret. A third-year resident asked for Merenstein's help with Gloria, a patient who suffered from lower abdominal cramping pain but had no other symptoms. Test after test came back normal, but her pain remained. After Gloria told Merenstein about her mysterious symptoms, he guided the discussion to her marriage, then to her sexual relations. Finally, Gloria opened up: She cried, explaining her husband's demands and her disappointments. Merenstein suggested they had uncovered something important and encouraged her to come back for more help with the resident.

"I simply gave her an opportunity to talk about herself and focus on the real source of her pain. I had no preconceived ideas," says Merenstein.

As Merenstein was mulling the creation of a new course on how to get patients to open up to residents, weeks passed. Gloria never came back. Nor did she return several phone calls.

To this day, Merenstein wishes he knew what he should have done differently: "Demonstrating psychosocial aspects of care without interfering with the relationship between resident and patient remains a delicate issue."

For years, Heidi Feldman has invited families of children with a variety of conditions to talk to her classes about their experiences with physicians. The first mother to present to one of Feldman's classes had a premature baby. The mother told her story, and when she talked about a conflict that she had with a doctor she'd say, *I would have preferred he'd done it this way. Or it would have been more helpful if ...* With presenters like this, Feldman's students were gaining excellent insight for how it feels to be the parent of a sick child and how they might communicate best as a doctor. Then one day, the father of a recently diagnosed child came to present. *Doctors don't listen. Doctors aren't helpful*, he said. Feldman cringed as the father attacked the medical profession. She watched her students tense up in their seats, listening to this angry man, learning little but what it's like to be unhappy. This kind of situation happens to Feldman rarely, perhaps with 2 percent of her class visitors. So Feldman remains committed to having her students hear firsthand from the parents and children they will serve. It may become charged emotional territory, yet it's certainly worth the effort.

One evening, a resident in the neonatal unit approached Gerald Merenstein with an idea for a treatment for a premature baby. Merenstein listened to the young physician's suggestion about using pulmonary vasodilators to open the arteries going to the lungs to help a child with underdeveloped lungs.

"What's the evidence for this?" Merenstein asked. The resident didn't have any evidence. It was a hunch.

About a decade later, pulmonary vasodilators are the standard of care for helping premature babies breathe. Merenstein laughs as he bemoans how he dismissed the suggestion; he wishes he hadn't quashed the young doctor's idea.

Carole Coffee and another teacher presented a junior high science class for broadcast to all of Oak Ridge, Tenn. The two planned to show a spontaneous combustion.

As the cameras rolled, the teachers dove under the desk to avoid the fallout from the explosion. Coffee, curious to see how the combustion was going, crawled from underneath the desk, not thinking about the fact that she was wearing a suit and panty hose, not thinking about how this image of her was being broadcast to classrooms throughout the larger metropolitan area.

As long as Coffee lived in the community she was exposed to the fallout from the explosion. Students would say, *Hey, aren't you that teacher who showed the spontaneous combustion? I remember you crawling around.* It proved to be an indelible image, but not one she would have chosen to contribute to her credibility among students and their parents.



Who Inspired Them

We asked top teachers, what teachers do you admire?

It was Gerald Merenstein's first night on call as an intern at Fitzsimons General Hospital in Aurora, Co., when a couple rushed in with their 11-day-old daughter. She was critically ill. Merenstein (MD '66) admitted the girl at midnight and stabilized her.

The parents had driven for most of the day and night from their home in Florida to bring their daughter there. "Can you call Dr. Plunkett?" they asked Merenstein. The couple knew pediatrician **Daniel Plunkett** from when he cared for their older daughter with anemia. Soon, Plunkett arrived and talked to the family, while Merenstein continued caring for their child. Merenstein couldn't believe that someone would drive all that way to see a doctor. Plunkett always said you have to care for and about the patient, and now Merenstein was able to see the devotion that could inspire.

The family soon moved to Colorado to be closer to Plunkett. But when he left Aurora, Merenstein became the children's pediatrician.

In Basil Zitelli's earliest memory of **Catherine DeAngelis (MD '69)**, she is an intern at Children's Hospital of Pittsburgh, soothing a fussy toddler so that a group of eager medical students can lay their hands on the child's chest, leaning in to listen for the rhythm of his heart. "She alleviated his fears so that we could learn," says Zitelli. DeAngelis (now a Pitt trustee and editor in chief of *JAMA*) taught by demonstration; her warm, easy manner seemed to calm even the most distressed child. Now a pediatric specialist, Zitelli has developed his own method of disarming and distracting his patients while obtaining practical diagnostic information—he thumb wrestles them. "It relieves stress," he says, "and allows me to assess their strength and motor skills." He's often surprised by their power; in his experience, the patient often schools the doctor.

Nicholas Cauna was a professor of anatomy and embryology at Pitt when Cynthia Lance-Jones first came to Pittsburgh. She remembers he could draw any embryo at any stage—with either hand. "His final drawings were often spectacular, but he always started out simple, so the students could follow," she says. When PowerPoint eclipsed the blackboard as a visual aid for lecturers, Lance-Jones fears many lost sight of the value of the latter's effectiveness. Many teachers are wooed by the beautiful pictures they can copy from textbooks or the Web, but in her lectures, Lance-Jones' touchstone is Cauna's elegant chalkboard renderings. Like Cauna, she takes the students on the journey with her, instead of just showing them pictures of their destination.

If the late Pitt surgeon **Charles "Chuck" Watson** asked you a question during rounds, says Jamie Johnston, you knew that he already knew the answer. He knew the literature better than anybody. But if you didn't know the answer, he wasn't going to tell you. You had 24 hours to find out. Johnston remembers Watson saying, "It's not a sin to say you don't know. But it is a sin to say you don't know 24 hours later." This principle taught Johnston never to be content with his own knowledge base. He says he thinks of Watson every time he tells a student or a patient "I don't know." "As a doctor, you are a lifetime student," he says. "It's your responsibility to find out."

James Ferrante (MD '65) was the longtime family practice residency director at UPMC St. Margaret. Joel Merenstein thinks that what really made him a great teacher was how well he got to know his residents and his desire to help them learn. He would sit in the preceptor's room (though he never really sat still for very long) and guide a medical student with gentle questions as she translated pathophysiology into patient care. He would tell a resident who was getting too dependent on his preceptors to "Go look it up yourself." He was a role model, displaying the care and personal touch appropriate for an elderly woman with multiple chronic illnesses and not much available treatment. And for residents who were getting a little too self-assured, he'd ask just the right questions to let them know they really didn't know enough yet.

Then, he would sit back and ask all of them about their spouses. He knew the names of everyone's children, as well as their grades, and in what activities they participated.

When Ferrante became ill with lung cancer, he used himself to point out to students and residents physical cues to notice. Ferrante died when he was 54. In his last days, he would leave his hospital room in his robe to attend medical conferences at St. Margaret; and he always added something to the discussion that no one else had considered.

When Nina Schor was a resident in pediatrics in the early '80s, she had an idea for a research project. She hoped to change the way doctors fought neuroblastoma, one of the deadliest tumors that can afflict the nervous systems of children age 4 or younger. Hers was a crazy idea out of the blue, as she puts it.

She needed a mentor and home base for her work. So she visited **Manfred Karnovsky**, professor in the Department of Biological Chemistry at Harvard Medical School. The work she wanted to pursue was not directly related to his lab's. But Schor wanted to apply his group's techniques to the clinical arena.

"I met with him, presented my ideas," says Schor. "A discussion ensued, and the next thing I knew, he showed me to my lab bench and laminar flow hood."

During the next three-and-a-half years, they met countless times.

"He was always available when I needed him; he was always nowhere to be found when I needed to be left on my own to do my own thing."

Schor's "crazy" idea is used as part of a neuroblastoma therapy today. ■

Their Tips, Tools, and Tricks

There's a method to their magic.

IT'S LIKE THIS "Think of the liver as a factory," R. Harsha Rao tells his students. "It makes a product—glucose—that it sends out into the yard, which is the blood. The horse and cart are the delivery system—insulin—that carries the product to the consumer, represented by the house, which represents every organ in the human body."

Several simple, hand-drawn cartoons appear on a screen. A factory spewing out black smoke, with piles of its product stored in the yard. A house. An animated horse and cart glide across the screen, delivering packages from the factory to the house.

Rao is describing to first-year medical students the concepts that underlie the metabolic changes in diabetes mellitus. The cartoons, drawn by Rao himself, explain how diabetes throws the body's finely balanced system of production and consumption into disarray. Rao's students may remember some favorite cartoons:

Type 1 diabetes: The horse is sprawled on the ground, obviously dead. There is no insulin, so packages of the factory's product pile up in the yard, which illustrates dangerously high blood glucose.

Insulin resistance: This time the house is set on a hill. The horse is normal, but it can't meet the delivery rate required because of the burden of going uphill.

Compensatory hyperinsulinemia: The image of the normal horse dissolves, and in its place is a caricature of the equine, twice as large as before, muscles bulging everywhere.

"If the horse you have is not strong enough to do the work, you have to go out and get… Arnold Schwarzenhorse," Rao says. Compensatory hyperinsulinemia is the physiologic equivalent of the "horse on 'roids"—higher insulin levels in the blood, in response to insulin resistance, Rao explains.

Arnold Schwarzenhorse and Rao's other cartoons have been fixtures in his cell science nutrition lecture since 1994. So notorious is the lecture that students who see him in subsequent years during their clinical rotations often say, "You're the one who gave us the Arnold Schwarzenhorse lecture!"

"All I can do," says Rao, "is shake my head ruefully and respond, 'Yes, but it's really the diabetes lecture!'"

Jamie Johnston also encourages his students to visualize everyday analogies for complex concepts: "I always try to use as examples things we're all familiar with, like driving a car." These real-world analogies also translate to the bedside. Later, students can rely on the same methods to explain concepts to their patients.

NEVER SAY DIE Physicians rarely allow students to manage crisis situations, says Paul Rogers. So his students spend an hour a day in the simulated intensive care unit at WISER (the Peter M. Winter Institute for Simulation, Education and Research), where the patient is a life-size mannequin whose vitals Rogers controls. If the mannequin is having trouble breathing, the student has to assess the situation quickly and make a treatment plan. The student might have to insert a breathing tube. But what if he can't get the tube in? In the simulation center, there's no attending to call for help. The dummy's blood pressure and oxygen level will drop, and the student will have to resuscitate. Rogers finds that his students learn quickly how to handle surprises. "They get to see in one month what I've seen in 25 years," he says. But in his class, the dummy never dies—Rogers will end the simulation before tragedy occurs. "I let it get uncomfortable," he says. He's found that when the mannequin dies, students tend to focus on the bad outcome and don't learn the objectives for that session.

WITH PLEASURE Georgia Duker keeps a *Prince Valiant* cartoon in her office. In it, one of the king's sons is in the library with his tutor, wistfully staring out the window at jousting knights. Then the boy runs outside to watch more closely. The caption reads: *Jeffery sets the boy free and remembers that what is learned without pleasure is forgotten without regret.*

When Duker lectures, she thinks about this cartoon and recalls that most students only have an attention span of 15 minutes, so she breaks up the class period. Sometimes she has students briefly engage their neighbors in a related discussion. Sometimes she has them write down their thoughts and tell them to her at the end of the class. These breaks keep the students actively engaged during long class sessions, she says.

WHERE'S THE PROOF? One of Gerald Merenstein's favorite mentors (besides his brother Joel Merenstein, who's also an award-winning teacher) always insisted he give evidence, before evidence-based medicine was in vogue. Today, Merenstein often asks students, "What's the evidence?" He'd like the field of medical education to hold itself to the same standards. He asks why, for example, more medical educators don't use adult learning theories to shape curricula.

THINK FOR THEMSELVES One summer, an undergraduate honors student was working in Nina Schor's laboratory. Schor asked the student to take a stock solution of a reagent and dilute it to use in an enzyme assay. The student came to Schor, calculator in hand, asking for the formula by which she should decide how much 10-molar solution and how much distilled water to use to make a .5 molar solution.

"There is no formula by which to do that," Schor said.

The student looked at Schor, dumbfounded.

"By what factor does 10 differ from .5?" Schor asked.

The student punched away at her calculator, then said, "20."

"Then that's the factor by which you want to dilute the stock solution. Dilute it 1-to-20."

"Is it 1-water and 20-stock solution or 1-stock solution and 20-water?" the student asked.

Schor paused. "Do you want to change the concentration by a lot or just by a little?"

"Oh," the student said, a little miffed. But she had caught the meaning of Schor's exercise. Schor believes the student actually accomplished much more through this circuitous route than if she had diluted the solution appropriately from the start.

Schor reminds us that a student's brain is often the best teaching tool. ■



What not to Do

These missteps will make you less effective as a teacher and role model, according to our top teachers.

Don't belittle, yell, intimidate, or embarrass. Instead, find ways to provide criticism without injuring self-esteem. Direct comments to the educational experience—what the class as a whole can learn—rather than the person.

Don't call medical students "kids." Give them the respect they deserve as adults.

Don't "pimp." That is, don't grill students for the sake of flaunting your own knowledge. (Put on a white coat, head out on rounds, and you're in danger of adopting the nasty habit of attempting to establish authority by quizzing others on lab values from 1963—among other obscure facts.) Pimping has nothing to do with patient care.

Don't let anyone get away with memorizing without understanding.

Don't go over the time limit of the class.

Instead of focusing on what you are teaching, focus on what the students are learning.

Don't spoon-feed.

Don't think that teaching is easy work—it takes passion.



LIGHTNING IN A BOTTLE

NEW ACADEMY OF MASTER MEDICAL EDUCATORS | BY JESSICA MESMAN



The student was halfway down the hall when Steven Kanter gave chase.

She'd stopped by the medical school vice dean's office to ask if he could recommend a good neurologist, a referral for a sick friend. But Kanter was in a meeting, addressing one of the dozens of administrative necessities that break his day into 20-minute increments. This one adjourned early—a rarity. When his assistant told him he'd just missed a student, he bolted and caught her just before the exit.

"What did you need?" he asked.

You might guess that he was breathless from the effort. But Kanter's gentle, measured demeanor seems unflappable. Go ahead, give him 20 minutes. You'll think you can accomplish anything.

"Oddly enough, it can be frustrating," says Cynthia Lance-Jones, an associate professor of neurobiology. Kanter entices faculty to do the impossible, to add one more helping to an overflowing plate.

"He brings up great ideas about teaching and student interaction," she continues. "You would like to have time to think about all of them, but often you just don't." These remarks come from someone who's no teaching slouch. Lance-Jones is a favorite teacher and an award winner for her contributions to the Pitt med curriculum.

With all the pressure on med school faculty to increase clinical and research productivity, their professional development as educators probably receives less attention than it should. The dean has laid out Kanter's newest mission: Capitalize on the teaching genius in our midst. Offer an environment that encourages the school's best educators to further develop their own ideas about teaching and mentoring and to build on the talents of others.

This academic year, the school will launch its new Academy of Master Medical Educators. The organization will be a think tank of the medical school's best educators. Similar organizations have shown up recently in Harvard Medical School, Baylor College of Medicine, and at the University of California, San Francisco. A recent article in *Academic Medicine* proclaims an "Academy Movement" is sweeping American medical schools. But most of those other programs focus only on medical student educators; Pitt's will extend across the spectrum of its faculty—recognizing those who teach med students, interns, residents, fellows, PhD students, and those who are part of continuing medical education programs.

"The boundaries between medical student education and resident education are person-made," says Kanter. Sharing ideas across the curriculum, and across specializations, is a way to improve the educational experience for everyone in the institution, he believes.

Currently, about 800 faculty members teach students in the School of Medicine. The academy, shepherded by six charter members, will honor about 50 of them. Nominees will be subjected to a rigorous peer review of their teaching, mentorship, research, and intellectual leadership. But what the school is really looking for are those who have contributed to Pitt's program in ways that are imaginative, creative, and innovative. For example, these teachers might have helped start a significant new program.

So once all the members have been invited, what exactly will they do?

The charter members will figure that out in the coming months. Right now, Kanter is just excited about the prospect of getting 50 brains in the same room to share ideas, whether for a seminar series or a social event or a mentoring session with junior faculty. These are some of the ways the school expects the academy will leverage faculty expertise in a more structured way.

There will be immediate benefits to members of the academy, including a prestigious honor to add to their CVs, a financial incentive, and a real opportunity to contribute to the educational mission of the medical school. Memberships will be eligible for renewal every few years based on teaching productivity. (Kanter refuses to use the term "teaching load": "You don't hear people talking about their 'research load.' It's a cultural issue in academia.")

That said, Kanter characteristically points out that the best teachers know the real reward is internal. Being in an academic environment, having direct contact with students every day, inspires them, he notes.

"Teaching is the most rewarding thing I can imagine," says Paul Rogers, professsor of critical care medicine and a multiple Golden Apple Award winner. "I teach a large portion of the graduating class to go out and be a better doctor than I was."

This kind of enthusiasm, in turn, inspires students. Send an e-mail asking Pitt med students to tell you a story about how their teachers have influenced or otherwise impressed them, and your inbox will soon be inundated.

We have the kinds of teachers, they'll say, that make you want to be a better student, a better doctor, a better colleague, a better person. The kinds of teachers who make others want to teach.

Some might say that trying to institutionalize that kind of charisma is about as easy as catching lightning in a bottle.

Kanter would introduce them to Pitt's new academy. ■

RETHINKING NEONATOLOGY

BY CHUCK STARESINIC

AT THE BOUNDARIES OF HOPE

For neonatologists, the most delicate and critical part of the job often comes before the patient—a critically ill infant—is even born. When a preterm birth is imminent, a neonatologist will talk with the parents about what to expect in the course of the next few hours or days as they become parents of a premature baby.

"Everyone thinks you just take care of babies," says Gary Silverman, the newly arrived chief of neonatology at Magee-Womens Hospital and professor of pediatrics in the School of Medicine, "but I can tell you right now that taking care of the children is only a small component of what we do. I think the biggest part of our work is taking care of the families."

ILLUSTRATION | VERA SIFFNER/CORBIS

The neonatologist's ability to offer these parents encouraging news has increased exponentially in the 40-odd years since First Lady Jacqueline Kennedy gave birth almost six weeks early to a son. Patrick Kennedy weighed about four-and-a-half pounds and survived only two days. "Today, that kind of baby is really a bread-and-butter baby for us," says Charles Bender, medical director of the neonatal intensive care unit (NICU) at Magee. "It's a routine baby." Even a baby born three months early and weighing a little more than a pound now stands a good chance of survival and, eventually, good health.

But when a baby is at the lower edge of this borderline of viability—born extremely early, with multiple complications, or weighing only a pound or so—Silverman will talk with the parents about expectations and possible outcomes.

For expectant parents, it is quite possibly the most heartrending experience of their lives. One day, they are six months into a normal pregnancy. The next, they learn that their baby will be born too early. Though the fetus is very much alive in the womb, the parents need time to grieve for the perfectly healthy newborn that they'd hoped to have. They'd anticipated this baby for so long, it's as though they'd lived with the child since before conception. They may have given her a name already and have probably always thought of her as perfect and complete. If this is an extreme case, a birth at say, 24 weeks of gestation, they will become the parents of a baby so tiny and light she will rest in the hand like a newborn kitten. The baby will have translucent skin as delicate as that of a ripe pear, eyes that won't open because the lids are still fused, and lungs unprepared for the air she must breathe to survive.

For some premature newborns, there is little or no chance, and this will become apparent within days. The newborn will be unresponsive—"neurologically devastated," Silverman says—which often indicates massive bleeding in the brain. Some may do well or survive with manageable disabilities, but only after extraordinary medical intervention and a protracted stay in the NICU. Others might survive but remain profoundly impaired, despite heroic measures. Silverman suggests to some parents that they may need to make difficult decisions as they go. If their baby is resistant to all treatment, then the parents, in consultation with the medical staff, may eventually decide that treatment should not continue.

All parents want the same thing, says Silverman. They want "everything" done for their baby. But what is everything?

All parents want the same thing, says Silverman. They want "everything" done for their baby. But what is everything? For some, it means weeks or months in the NICU and prayers for a long and healthy life. For others, whose babies don't respond to treatment, it means providing relief from pain and discomfort, wrapping the baby in a blanket, and allowing the parents to cradle her until she ceases to breathe. For parents about to deliver a premature baby, the neonatologist describes the boundaries of hope.

Most of these expectant parents will take on a long and difficult struggle that ends in success. Some will witness the briefest of lives.

And less commonly, some will become loving caretakers for a child who lives to adulthood and is never able to sit up or feed herself.

"It doesn't happen to all the children," says Silverman. "I give them percentages, and I tell them that percentages don't matter if your child falls into that group—it's 100 percent for your child."

It's a slow day at Magee's NICU—only 42 babies on hand—which means that Charles Bender has a few moments to talk. His brown hair is neatly combed and touched with gray. He wears a blue shirt and a bright red tie spotted with dogs, cats, raindrops, and umbrellas. Despite the perky attire, he seems a bit weary as he walks the wide hallway of this newly opened NICU, until he's asked to describe what goes on here. "We save babies' lives," he says without hesitation. A smile lights up his face as the thought consumes him. "There can't be any greater reward."

The new NICU is as colorful as a preschool. Its design incorporates lessons learned at Pitt and elsewhere that show a direct connection between the quality of the environment and the health of the baby. Patients get single rooms, each defined by three walls and a long curtain. As long as the baby is in the NICU, this room is the family's turf, where they can feel a measure of privacy, where they can bond with their baby, speeding his development into a healthy infant that can go home. Magee's NICU will be able to accommodate 48 newborns in this way by January (plus 15 in other ward beds). Bender describes the traditional model of the NICU, which is still in use in many hospitals, as "the television model." There are lots of babies together in one room, each in its own incubator. There are bright lights, beepers and buzzers, and lots of commotion.

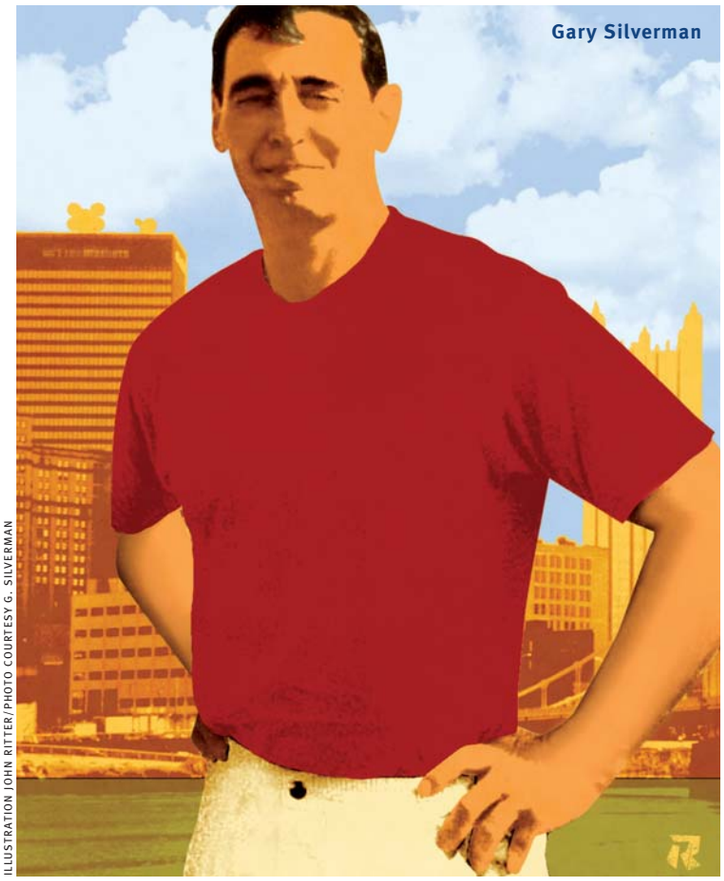
"It makes a great television set," he says, "but it makes a horrible place to be when you are sick." About six years ago, the staff at Magee began to change the environment by dimming the lights, cutting down on unnecessary noise like the radio, and simply lowering their voices. Within a month, Bender says, they cut the use of sedation drugs by more than 50 percent, because the babies showed fewer adverse reactions that required sedation. Babies came off the respirators sooner, ate more readily, gained more weight, went home earlier, and began to show age-appropriate interest in their environment rather than hostility toward it.

Silverman arrives at Pitt as the School of Medicine's new chief of the Division of Neonatology and Developmental Biology, having witnessed this evolution of NICU design in the past 20 years or so in NICUs at Washington University (St. Louis Children's Hospital) and Harvard University (Children's Hospital Boston). Insights learned in the NICU have made his work at the laboratory bench stand out.

"Gary is one of a rare breed of pediatric scientists," says David Perlmutter, chief physician and chief scientist at Children's Hospital of Pittsburgh and chair of pediatrics in the School of Medicine. "He is an MD/PhD who is both superb as a clinician and competitive as a scientist at the NIH [National Institutes of Health]. There are very few academic pediatricians who are competing successfully at the NIH while still involved in the clinical enterprise." In neonatology, he says, there are even fewer prominent physican-scientists than in most pediatric subspecialties, perhaps because the field has flowered relatively recently.

F. Sessions "Sesh" Cole, the neonatologist who was Silverman's clinical mentor at Washington University, puts the number at "fewer than six people around the country like Gary." (Cole counts himself among that handful of scientists who are also clinical neonatologists.) "One of the only ways that we're going to be able to care for babies better five years from now … is by bringing fundamental discovery research to the bedside. And Gary is one of the few people around the country who is genuinely able to do that."

As a freshman at Washington & Jefferson College, Silverman appears to have been equal parts science prodigy and typical adolescent. The Youngstown native chose the



Gary Silverman

ILLUSTRATION JOHN RITTER/PHOTO COURTESY G. SILVERMAN

small college in Washington, Pa., over others for one reason: They told him he wasn't too small (about 5-foot-9) to make the football team. For a kid who'd figured his football career ended with high school, that was the clincher.

That first year, he showed up unannounced at the office of Dennis Trelka, head of the biology department, to ask him to be his adviser. This would have been an unmitigated indication of Silverman's maturity if the discussion hadn't quickly turned into an argument. The freshman wanted to do an honors project in biology. Trelka said that wasn't possible. No student had ever done that before the junior year. Silverman was insistent, and Trelka finally suggested he might want to come back at another time, when he was ready to discuss this in a more effective manner, because he was not going to win this case. Furthermore, maybe he should consider asking someone else to be his adviser, because the two of them didn't seem to be hitting it off.

Silverman did come back another time, still wanting the head of biology to be his adviser. (He liked the fact that Trelka looked him in the eye and laid down the rules.) The eventual compromise was that Silverman would do his honors project as a sophomore. Throughout the next few years, Trelka would occasionally visit Silverman at Hahnemann Medical College (now Drexel) in Philadelphia, where Silverman had arranged to do summer research. The two have been close friends ever since.

Silverman was quite an athlete, admits Trelka. He was quick and coordinated, a four-year starter at cornerback and a track athlete who broke the college's pole-vault record. "But he was a better student than a football player," Trelka says with a hearty laugh. "And I would say that even if he were in the room."

As an undergrad, Silverman didn't know much about being an MD, except that it was a way to get into the sort of science he wanted to do—he was interested in immunology and cancer. He applied to a highly competitive physician-scientist program at the University of Chicago Pritzker School of Medicine. Eight applicants were accepted, he learned, and he was number nine. When one of those eight opted to go elsewhere, Silverman squeaked in. At Chicago, he worked in the lab of Richard Rothberg, head of pulmonary medicine at the pediatric hospital. Occasionally, Silverman would have to track him down in the cystic fibrosis clinic to discuss lab results. "I'd find him on the wards," Silverman recalls, "and I would watch him interact with families and patients. ... I don't think I've ever seen anybody as gentle with patients and families as he was. I think that had a pretty big influence on me."

Rothberg pushed Silverman into pediatrics simply through his example. He also told him, without explanation, that he needed to spend part of his career at Children's Hospital Boston, so Silverman applied for a pediatric residency there. He planned to pursue a fellowship there as well, in hematology-oncology. But in his third year of residency, he ran into a dilemma. He was in the fellowship director's office, being offered the hematology fellowship, but he couldn't sign the papers. Somewhere in his pediatric residency, he'd become intrigued by the incredible complexity of taking care of newborns. It was a critical care subspecialty, but it included this fascinating element of developmental disease. "Here," says Silverman, "you had this rapidly developing organism, and the diseases you were seeing were related to disorders of development, either acquired, because the child was born prematurely, or constitutional—there was some genetic component to it. And that's when I finally made my break with immunology, because I saw that and thought, *This is really fascinating!*"

Silverman went to see the director of the neonatology fellowship, Sesh Cole, and told him that he couldn't sign the hematology fellowship papers. That's good, Cole replied, because you really need to go into neonatology. In part, Cole wanted to recruit this promising scientist to his own field, but he had also watched the young resident in the NICU, and he saw the spark of interest. Silverman knew he was right. Neonatology was "one of the last frontiers of pediatrics," he says.

Cole soon relocated to Washington University in St. Louis, where he continued to mentor Silverman as a clinician. There, Silverman joined the laboratory of Stan Korsmeyer, whom Perlmutter refers to as "one of the best physician-scientists in the world." Korsmeyer had discovered the BCL-2 gene was mutated in certain types of cancer, and realized that the gene was fundamentally important to the control of apoptosis, or programmed cell death. This was the beginning of the modern era of apoptosis cancer research, which continues to this day.

From 1988 to 1991, Korsmeyer had Silverman build a map of the long arm of chromosome 18, which is where BCL-2 is. To do this, Silverman worked with genetics pioneer Maynard Olson in what was really the forerunner of the human genome project. Olson manipulated yeast to replicate DNA, creating the first means of mapping human chromosomes. In the course of investigating chromosome 18, Silverman stumbled upon several genes for a class of proteins whose function was a mystery. Today, these proteins are the focus of the laboratory that he brings with him to Pittsburgh. They appear to be keys that will open up a whole new understanding of basic cellular functions and possibly lead to new life-saving treatments for the tiniest of patients.

Silverman's lab has zeroed in on a group of proteins known as serpins. They are protease-inhibitors, so they stop the action of specific enzymes. Many serpins are well studied and their functions understood. Silverman's new boss, Perlmutter, for example, studies a serpin that, when inherited in a mutant form, causes a type of liver disease in children. One member of this serpin family inhibits an enzyme that attacks the lung. Others inhibit the clotting pathway. These proteins circulate in the blood-

stream, regulating essential biological functions.

Silverman's serpins look similar, but they have at least one major tantalizing difference—they are not secreted into the bloodstream at all. For some reason, they are inside our cells. Silverman's lab has already published evidence that one group of these serpins inhibits intracellular proteases, which he likens to molecular scissors that can injure cells. Programmed cell death is triggered by these scissors.

By knocking out individual serpin genes in the nematode worm *Caenorhabditis elegans* (see "Family Portrait," below), Silverman is discovering that the proteins play important roles in basic cellular functions—he says that biologists never dreamed that serpins were involved in these processes. For example, when a cell is exposed to high salt concentrations, it shrinks, and before the cell gets damaged, it corrects itself and takes up water to return to its normal shape. Conversely, if the salt concentration outside the cell drops, the cell takes on water and swells. Normally, the cell controls the swelling before it ruptures. In worms with certain serpins knocked out, the cells are unable to adjust to these changing conditions and they die. Silverman thinks that these serpins inhibit intracellular proteases that kill off the cell when conditions change. Adjusting to changing salinity is one of the most basic cellular functions that all living things must perform. A lot of diseases are associated with changes in cellular volume, says Silverman. Diarrhea kills countless children worldwide through dehydration. In diabetic ketoacidosis, dehydration leads to cellular injury and death. In congestive heart failure, cells take on too much water. Serpins may be key to controlling these processes and mitigating the damage.

Other serpin genes appear to play a role in responding to bacterial infection. Many infectious organisms use proteases themselves to either gain access to the cell or gain access to the body. They break through barriers to get into cells. They use their own proteases or they activate proteases of the host to survive and evade immune surveillance.

Silverman thinks that physician-scientists could learn to manipulate serpins to enhance protection against infection, possibly even in newborn patients. Some preliminary data suggest that serpins protect the lungs against protease-mediated injury. It looks like much of the chronic lung inflammation that premature babies suffer could be due to proteases. The serpins he is studying are highly expressed in the lungs but are not turned on yet in premature infants. Silverman can imagine a therapy that turns on the genes so that the body produces the serpins or another that actually provides such proteins to premature infants, delivered via the bloodstream or as an aerosol directly into the lungs—custom-made serpins for what ails you.

Silverman's erstwhile mentor, Cole, predicts that these discoveries will lead to dramatic changes in treatment—perhaps providing therapy in fetal life, through the mother.

Though he knows that Silverman entered medicine for the science, Cole remembers him for the way he has embraced both roles of the physician-scientist. One night in particular, amid the worst ice- and snowstorm of a Missouri winter, Silverman took a transport call in the NICU. A physician at a suburban hospital had an infant in serious trouble. He needed his patient to be transported to St. Louis, a two-hour trip, where more specialized care was available. Silverman worried for the safety of the ambulance crew and the infant should anything go wrong on those icy roads. He made a few telephone calls and arranged for a state trooper and a snowplow to escort the ambulance to St. Louis. Somehow, he was able to convince the powers that be that, though the plow driver and the trooper were probably busy this night, shepherding this baby to the hospital was the most important thing they could do. So, for the next few hours, the plow cut through the snow, and flashing lights pressed on through the stormy darkness, slowly pushing back the boundaries of hope. ■



COURTESY SILVERMAN

In a close-up of the worm *C. elegans*, a newly discovered protein glows green where it is expressed. Worms overexpressing this protein experienced developmental abnormalities (white arrow), suggesting a critical role for such proteins in development—perhaps of humans as well as worms.

FAMILY PORTRAIT

Most people don't feel much kinship with worms, but medical researchers often look at life from a different perspective.

Gary Silverman, Pitt's new chief of neonatology and developmental biology, spends a lot of time thinking about the tiny nematode worm, *Caenorhabditis elegans*. He'll point out that at the cellular level, we're a lot like *C. elegans*. There are certain processes in humans that can't be studied in the worm, but Silverman is interested in how cells react to various stresses—for that, the 1-millimeter worm is ideal. It reproduces quickly and has a hermaphroditic form that permits selfing—producing worms with the same genetic makeup. The fate of each cell from the zygote to the adult animal is known. The neurological pathways are completely mapped out. To top it off, the worm is transparent, so changes in development are easily observed.

Silverman has found genes for the proteins he studies in creatures as divergent as worms, humans, and even jellyfish, meaning these proteins were probably present in the primitive multicellular creature that was ancestor to us all. Through millions of years of evolution, the ability to produce these proteins has been conserved, presumably because they serve basic and vital cellular functions.

When Silverman started mapping human chromosomes 15 years ago, it took years to identify such shared genes. Now, he says, it takes about 15 minutes. "That's why work that we do on something as fundamental as *C. elegans* can have immediate clinical import to a 700-gram baby that's sitting in the NICU at Magee," he says. "You can discover a biochemical pathway in a very simple organism and then sit at your computer and determine whether or not any of those proteins exist in humans.

"You're going to find enough clues there to be able to ask pretty relevant questions in mammalian or human systems pretty quickly." —*CS*

WHAT KEEPS MD/PHDS HUMMING THROUGH 8 YEARS OF MED AND GRAD SCHOOL?

(AND THAT'S NOT COUNTING RESIDENCY)

BY MEGHAN HOLOHAN

PORTRAITS BY FRANK WALSH

A few years ago, student David Volk walked into Western Psychiatric Institute and Clinic and headed up to the ninth floor—the schizophrenia ward.

As soon as he arrived, he was told to help with James Morris' diagnostic interview.

There's a metal surveillance bug implanted in my left leg, which travels around my body transmitting information, Morris told Volk instead of answering the question he was asked.

I used to play in the WNBA, but Michael Jordan has kept me from being a superstar, he said.

Morris wasn't making any sense. His paranoid and grandiose delusions strongly suggested a diagnosis of



"I might have been the only person to have chosen pathology having never done any pathology," Clayton Wiley says, laughing a little. He'd like Pitt MD/PhDs to plan their careers more intelligently.

schizophrenia. Other than that, all Volk knew about Morris he had learned from his intake records. The previous night, Morris (not his real name) had been on the streets of Pittsburgh screaming at people passing by. He'd been erratic, threatening. His behavior landed him in WPIC's emergency department.

The staff in the ED wanted to admit him. Morris refused. *I don't need to be in the hospital. I can stay with my father.* He struggled as he was involuntarily admitted.

It didn't seem like Morris had been eating. And the rags that covered his lanky frame indicated that he might not be able to care for himself. Morris had probably been living on the streets.

After being interviewed by Volk for a while, Morris started crying.

"I just want to go home."

Home was his father's house, Morris insisted. Yet, Morris didn't know where his father lived. Volk (MD/PhD '04) thought that Morris might feel better if he could return to his father's place. A patient man of medium build with gold-rimmed glasses, Volk had just started his psychiatry rotation. He'd spent the past five years doing schizophrenia research in the lab of David Lewis, professor of psychiatry and neuroscience. Now he was meeting a fellow man who had the disease he'd studied in such detail. Morris was exactly the kind of person Volk wanted to help with his research. Here at the hospital, instead of examining diseased brain tissue, Volk was witnessing a manifestation of all those things he had studied—a person with a complex, debilitating, lifelong disorder.

Morris was the "translational element" that Volk had heard so much about as an MD/PhD student at the University of Pittsburgh.

The number of physician-scientists is decreasing in the United States during a time when research funding from the National Institutes of Health (NIH) for physicians who conduct basic science research has doubled since 1998, says Clayton Wiley, director of neuropathology and the MD/PhD program at the University of Pittsburgh.

"Biomedicine has become a much more complicated science," Wiley says, explaining that in the past 50 years, new fields such as molecular and structural biology have emerged. And the amount of medical and scientific information has grown exponentially.

When Jonas Salk's team scrambled for a killed polio vaccine, they were working with a "fairly simple disease," albeit deadly, notes Wiley. To make the vaccine, they had to replicate the virus. In the face of the modern HIV epidemic, scientists will draw on the enormous advances of the past few decades. To develop a vaccine, they'll need to understand the genes of the virus and how the virus interacts with the host. Likewise, scientists are, of course, using these tools to tackle age-old puzzles of medicine, like the herpes virus.

Wiley believes MD/PhDs, in particular, can play a valuable role in this scientific landscape. They're specifically trained to handle the depth and details of basic science research and translate those into practical bedside care.

He notes that the Association of American Medical Colleges has invited MD/PhD programs to be more actively involved in the organization because the association realized that physician-scientists are increasingly becoming leaders in medical education.

"A lot of institutions think of the MSTP [medical scientist training program] as a seed," says Bert Shapiro, a PhD who directs the medical scientist training program of the

National Institute of General Medical Sciences (NIGMS) for the National Institutes of Health. "It is a good way to get triple-threat faculty members who know medicine, research, and are good academicians."

There are 120 MD/PhD programs in the United States, and the NIH has selected 39 programs to support in light of the strength of those institutions' research programs, among other criteria. The NIH list includes the University of Pittsburgh School of Medicine program, founded in 1983.

The agency funds about a fifth of the students at Pitt. The School of Medicine finds money to fully fund the other students. Since Wiley took over the program eight years ago, the number of students has increased from four to 12 in each entering class. Without support from the NIH or the school, those MD/PhD students—who go to school for an average of eight years before starting their residency training—would graduate at least a quarter of a million dollars in debt.

"The crucial thing here is getting people early and giving them a chance to get thoroughly trained. You get highly accomplished and motivated researchers," says Shapiro, who is also branch chief of cell biology at NIGMS. Even though MD/PhD students have a lot of experience, they typically are a couple of years behind on the career ladder. Wiley notes the average physician-scientist gets a faculty position at the age of 37 and first investigator award from the NIH at 44. He is hoping that with new curriculum changes going into effect, Pitt students will be able to graduate in seven years and get into the workforce earlier.

Wiley pursued his degrees in the early days of physician-scientist training programs. After completing his undergraduate degree at the University of Chicago in 1976, he headed to the University of California, San Diego, to attend its MD/PhD program. His experience is similar to many who've matriculated through such a program. He completed two years of medical school, then spent four years doing neuroscience research, and when he finally returned to med school he was overwhelmed. He'd had no clinical training for four years. And his first rotation was surgery. Shortly after he started, he received a note:

"Dr. Wiley is a concern to the Department of Surgery."

It was difficult for Wiley to finish that rotation. He didn't understand the surgery residents, and they didn't understand him. He'd just spent four years devoted to the specifics of scientific investigation, asking the same question over and over in different ways to yield the best response. Suddenly he was expected to think like a clinician—to come up with an answer on his feet, then and there, with little time for weighing options. It was not a smooth transition.

It was the summer of 2002, 4:30 in the morning, and David Volk's alarm clock was squawking.

He pulled himself out of bed to get ready for his surgery rotation. He felt like he had just closed his Lawrence's *Essentials of General Surgery,* but that was at midnight. Ahead was another morning of relentless questions about the mechanisms of wound healing or some other clinical subject he hoped he could remember. Just a week before, as a researcher, he'd been contributing to the emerging body of knowledge about cognitive dysfunction among schizophrenic patients. But this morning, he was a third-year med student and a surgery newbie. All that he knew about schizophrenia would be of little help.

Volk felt much like Wiley did at the start of his surgery residency—there is some disconnect between being a PhD student and being a medical student.

But Wiley and his staff are making the disconnect less palpable. Students in the MD/PhD program at Pitt can participate in longitudinal clinics while they pursue their doctoral research. Spending a half day each week in the clinic helps sharpen fledgling doctoring skills. In addition, students can now dive into an eight-week clinical rotation after their second year of medical school, before they start their research years.

Fortunately for Volk, he was in the first class of MD/PhD students to benefit from these clinical programs. NIH's Shapiro expects that longitudinal clinics like Pitt's will become a trend. Both Pitt and the University of California, San Diego, have incorporated clinical experience during time typically allotted for doctoral research—and that approach is all the buzz at national meetings of MD/PhD program directors.

Wiley readily admits that his experience in a physician-scientist program informs how he has helped Pitt's program evolve. After being dumped into a surgery rotation, Wiley only had three months to decide what specialty he would pursue. He knew that surgery wasn't his calling but wasn't sure of much else.

"I might have been the only person to have chosen pathology having never done any pathology," he says, laughing a little. Wiley is a tall man with perfectly placed brown, silver, and gray hair. He folds his hands when he talks.

He thought pathology would be a good match with the graduate work he'd pursued in neurology.

"It was not intelligent," he admits about how he chose to specialize in pathology. "It was more luck than planning."

Sitting in his office more than 20 years later, Wiley makes it seem like there was little thought behind his career choice. In fact, almost every Pitt MD/PhD student makes the program seem like it is easy—like it is just a matter of perfect planning. And that certainly

YOU'VE GOT A FRIEND

When Genevieve Gorny's fiancé broke his foot, she didn't know how she was going to move her furniture by herself to her third-floor apartment. She had just moved to Pittsburgh from Duluth, Minn., to start the University of Pittsburgh School of Medicine's Medical Scientist Training Program. She hardly knew a soul in Pittsburgh, but she knew Russ Traister, a second-year grad student in the program who'd been assigned as her student mentor. Gorny had been paired with Traister because they shared an interest in biochemistry and molecular genetics. She stayed at his house when she visited campus, and he told her about all the great restaurants. Soon, he was at her service again, helping her lug a couch and heavy desks up the steps of her Highland Park apartment building.

The Pitt MD/PhD program prides itself on its student community. Students may pursue a wide range of studies, but they're brought together through their service on program-wide committees, with plenty from which to choose: There's a committee that organizes the annual retreat, one that interviews prospective students, one that organizes a weekend for visiting applicants, and then some. Student mentors don't just give advice on great hangouts; they are resources for finding a good preceptor for a longitudinal clinic or figuring out how to handle those first years of med school. And the student community, Gorny points out, is one of the reasons she decided on Pittsburgh. *—MH*



Patient interaction kept the scholarly fires burning for David Volk as he pursued eight years of medical and graduate school.

enters into it.

"The biggest question is, 'How does one person do two jobs?'" notes Wiley.

To help students figure out how to juggle two professional lives, Wiley has added advising sessions to the program since he assumed its directorship in 1996. As a student, Wiley didn't have the opportunity to meet with career counselors or a mentor specially appointed to guide him. However, at Pitt, each student is paired with a career adviser and a research adviser. While some students joke that they are advised to death, most of them agree that the counseling helps.

Shapiro rattles off a list of Pitt's strengths as a physician-scientist training program, including a large pool of applicants, which has increased during Wiley's tenure from 40 applications to 300 every year. He also mentions Pitt's nationally recognized programs like neuroscience, cognitive neuroscience, biomedical engineering, and transplantation. He lauds Pitt's partnerships with Carnegie Mellon University, enabling the training program to take advantage of CMU's strengths like robotics and social and decision sciences. (About 5 percent of Pitt students are pursuing less traditional MD/PhDs in fields like public policy.) But the quality Shapiro mentions first: "They have a very strong staff. Clayton Wiley is outstanding as a leader and role model."

Planning and clinics help, still the patients they work with are often the biggest motivators for students, as Volk has found.

When Morris first arrived at WPIC, his appearance and his smell—which was so penetrating that several showers and new clothes couldn't disguise it—indicated that he'd been living on the streets for some time. Volk knew it would be easier for Morris to live with schizophrenia in a home with a caring guardian. So he tried to track down Morris' father, which wasn't easy. Morris didn't know his father's phone number. And he wasn't sure where his father lived.

Morris, caught in the middle of a psychotic episode, was unable to understand why he was in the hospital. He was agitated all the time. He was disheveled. Yet, he inspired Volk. "During my MD training I did a lot of work with people who were suffering. I want to find a way to ease that suffering," he says, looking back on his experience. Pitt administrators note that PhDs with MDs tend to keep their research focused on the human element more than other PhDs might.

Morris had decided not to take green pills; he was convinced that green pills were poisonous. So the WPIC staff searched for a medication that wasn't green but would help Morris. He'd been taking four milligrams of the antipsychotic risperidone; the two-milligram doses were red. So Morris was given two red pills, instead of one green one.

Red or green aside, there's no cure for schizophrenia. But often doctors can help patients manage symptoms of the disease, like psychotic delusions. Still, risperidone and other medications do little to manage other symptoms, such as impaired communication and cognitive skills, including the ability to organize thoughts.

Meeting Morris reinforced Volk's thoughts about the limitations of current treatments. It demonstrated how meaningfully his lab pursuits could change people's lives.

The entire four weeks Volk was at WPIC, Morris never recognized him, nor did he recall that Volk was a medical student.

This is almost exactly what Volk was trying to understand through his research. Why couldn't Morris remember him? What is different in the brain of a person with schizophrenia that obstructs memory?

Volk became interested in the brain and how it works after taking an undergraduate class in neuroscience. Then he came to Pitt as a Baylor University senior to complete a summer neuroscience research fellowship, a 10-week program that gives undergraduates an opportunity to pursue neuroscience research with a faculty member. He worked in David Lewis' WPIC lab studying abnormalities in the prefrontal cortex in schizophrenic patient brains. Lewis ended up becoming his PhD adviser.

Studies have shown that inhibitory neurons in the brain play a role in complex cognitive processes, like short-term, or working, memory. People with schizophrenia have impaired working memory. Volk's doctoral thesis examines the role that GABA (gamma-amino butyric acid) plays in the brains of people who suffer from schizophrenia. GABA is a neurotransmitter that influences memory formation in the brain, Volk notes.

To better explain what he is describing, Volk grabs a notebook and draws a diagram of neurons. On his left hand is a wedding band. (He met his wife, who is now a physician's assistant, in a lab, though he still argues that students in the medical scientist training program aren't cloistered in labs and libraries, despite what you might assume. In fact, Volk mustered enough spare time to teach Bible study classes at his church, play sports, and set out on an occasional camping trip.)

On the notepad, Volk draws a circle with lines coming out of it, like a sun a child might color. *This is the chandelier neuron.* Volk connects the circle to a triangle. *A GABA receptor.* He explains further: Volk learned during his doctoral work, by studying the prefrontal cortex, that the brains of patients with schizophrenia don't appear to use GABA the same way healthy people's brains do. When he looked further, he discovered an important subpopulation of inhibitory neurons, called chandelier neurons, were particularly affected in schizophrenia. Those abnormal chandelier neurons could be the key to cognitive problems experienced by those with schizophrenia.

Volk continues to be fascinated with schizophrenia and hopes to continue studying it after he finishes his WPIC residency.

Whatever is responsible for disrupting the memories of schizophrenic patients, Volk witnessed the consequences firsthand as he got to know Morris. Occasionally, Morris would remember a tidbit about his life that Volk could use in search of the patient's father. Then after weeks of searching, Volk found the right phone number. When he called, Morris' father told him that his son hadn't lived with him for more than 10 years. And to Morris' surprise, his dad had remarried. Unfortunately, Morris wouldn't be able to live with his father and his father's new wife.

Volk soon finished his WPIC rotation and lost touch with Morris. Six months later, he started a rotation at Mayview State Hospital in Bridgeville. As he rounded one day, he saw a familiar face in the long-term mental care facility. It was Morris.

This time Morris was taking his medication. The stable, long-term environment clearly helped his condition. He was healthy and happy, no longer suffering from delusions. With regular medication, Morris could think a little more clearly.

Curiously, and to Volk's delight, Morris even recognized him. ■

CLINICALLY RELEVANT

As Lou Ghanem enters the Hillman Cancer Center, he sets down the dozen bagels he's carried in and looks at the patient lineup and progress reports. In the pocket of his white coat is a stack of note cards inked with information about the major causes of chest pain, details of clinical trials, among other facts he'd like at his fingertips in this clinic. He was nervous when he first started this clinical rotation.

It had been three years since he'd seen patients.

Ghanem is in his fourth year of the PhD segment of the medical scientist training program at Pitt. Today he is participating in one of two required longitudinal clinics, working with Suresh Ramalingam, assistant professor of medicine, in a lung cancer clinic. As soon as Ramalingam, whom his patients affectionately call Dr. Ram, enters the office, he begins peppering Ghanem with questions: "What are the major causes of chest pain? What are the different types of aneurysms?"

One of James Luketich's assistants pops into the room. Luketich—director of thoracic surgery and codirector of the lung center at Hillman—has a patient with a new case of lung cancer. He thinks the tumor has metastasized, and he wants Ramalingam to consult and take over as the oncologist.

Ghanem and Ramalingam look at the CAT scans. Then the two join Luketich in a room where the patient, Christopher Downy (not his real name), sits in a chair beside the exam table. Ramalingam sits beside him and gently questions him: "How do you feel? How is your breathing? Are you coughing? Do you feel differently than you did a year ago?"

After Downy answers the questions, he looks at Ramalingam and asks, "How bad is it?"

Downy's wife is sitting in the corner, balling up her fists, trying not to cry.

"I don't know yet," the physician answers.

Ghanem and Ramalingam return to the office, where Ramalingam confesses that he isn't feeling optimistic.

"If it's two primary tumors, can surgery work?" Ghanem asks.

"The question is, can he live with one lung?" Ramalingam says.

As Ghanem watched the doctor's compassionate interaction with Downy, he was torn. He wanted to observe, so that when he starts treating patients himself he'll know whether a hug or a handshake or encouraging words are the best way to comfort a patient dealing with a tragic situation. Still he was sad to be part of such a grave diagnosis.

Pitt is one of the few schools in the nation offering longitudinal clinics where MD/PhD students can practice clinical skills while pursuing their PhDs. That's likely to change, however, because word has spread about how valuable such clinics are for these students. At Pitt, each student takes two clinics. For each clinic, the student spends half a day each week for six months in a rotation, which is often more specialized than the typical med school rotation. Ghanem is pleased he can work in hematology and oncology.

"You can ask more clinically relevant questions [in the lab] if you have medical knowledge," Ghanem says. He works in the lab of Richard Steinman. With Steinman, an MD/PhD and faculty member in the Departments of Medicine and of Molecular Genetics and Biochemistry, Ghanem studies the mechanisms of normal white blood cell differentiation in leukemia.

Equally important to Ghanem, who suspects his clinical skills have lapsed somewhat: His time in the longitudinal clinic levels the playing field with his peers who are working on their MDs full-time. *—MH*

NOT ALONE

FOR NEARLY 25 YEARS, LILI PENKOWER HELPED STUDENTS WORK THROUGH IT

BY HATTIE FLETCHER



Penkower showed students that their problems had solutions.

COURTESY PENKOWER

As director of the Medical Student Counseling Program from its start in 1980 until her retirement in July, Lili Penkower knew more than a third of medical students at the University of Pittsburgh rather well. Often she learned things about them known by no one else—including their teachers, parents, close friends, and even romantic partners. When she saw these students around campus, however, she had to pretend they were strangers; a simple greeting might have undermined her effectiveness.

Penkower, a slender woman who doesn't look old enough for retirement, was a model of discretion. Her office, where you'd find comfortable couches and a dish of chocolates on the coffee table, was tucked away in a nondescript building on Fifth Avenue, off a medical student's normal path. She didn't want anyone to worry about being spotted on the way into or out of a session.

Despite her remote location, Penkower, who radiates enthusiasm and empathy in equal measure, had a strong presence on campus. She introduced herself to students during orientation and helped them anticipate the kinds of problems they might encounter. She also led a couples' meeting to discuss the impact medical school can have on relationships.

When students sought help with problems, she accommodated their schedules, taking more than her fair share of distraught, middle-of-the-night phone calls.

In Penkower's lexicon, "problem" means "anything getting in the way of the work students came to medical school to do."

At most medical schools, students seeking help head to the university's general counseling service. At Pitt, the program is tailored to med students' needs.

The issues she helped students deal with were typical for any 20-something population. They ranged from eating disorders and depression to family issues; these were often compounded by the pressures of academic life and staggering student loan burdens. She says one of her biggest jobs was helping overwhelmed students see that their problems had solutions. She never let a student walk out of her office without feeling a bit of hope.

One student, who asks to remain anonymous, thought she had a good handle on medical school and a strong support system—she was enjoying the experience tremendously. Then one day she hit a wall and found herself barely able to drag herself to school, though she ended up at an adviser's office. He immediately called Penkower, who met with the student that day and regularly throughout the next two months. Soon, the young woman was back on track.

"I honestly do not know what I would have done without her," the student says now. "I don't think I would have been able to bounce back into third year. She saved me."

The student learned to embrace a central Penkower tenet: You should learn to take care of yourself before beginning a career that requires you to care for others.

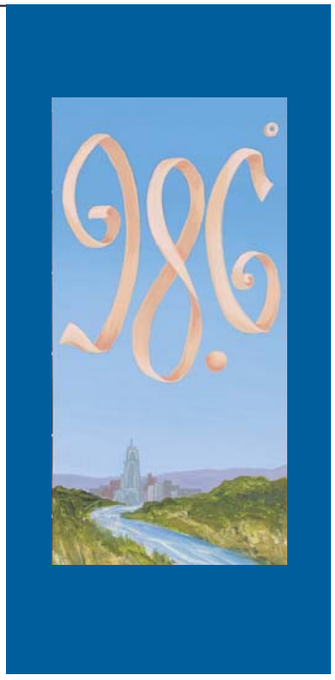
During her years at Pitt, Penkower was a graduate student (she earned an MSW in 1974 and a PhD in epidemiology in 1986), researcher (focusing most recently on adolescent transplant recipients), and (to the surprise of some students who first came to know her in the Fifth Avenue office) a class instructor. Among her titles: assistant professor of family medicine and psychiatry. She worked with various student groups on peer counseling projects, hotlines, and wellness programs.

Still, the student counseling, which she calls "the best thing I've ever done," always came first.

Penkower has moved to California, to be closer to family. She knows the program is in capable hands. Lee Wolfson, the new director, had filled in for Penkower during vacations. Wolfson, who has focused his recent career on depression in geriatric patients, enjoyed the experience of working with med students so much that when Penkower returned from a trip to Los Angeles last winter, he jokingly told her to keep him in mind if she ever decided to retire, not realizing she had been house hunting. Now he's working with students full-time.

And Penkower envies him that, a little. But she's giving herself some time to figure out what to do next—while learning how to deal with the stress of L.A. traffic. ■

People and programs that keep the school healthy and vibrant



HE KEEPS SHINING

A LITTLE ELBOW GREASE AND A LOT OF HEART

BY MELANIE DONAHOO

At 7:30 on a Tuesday morning, the fourth-floor hallway of Children's Hospital of Pittsburgh is quiet, save for the occasional brisk passage of a nurse or the hum of medical machinery. Then, an elevator door opens and a man in a worn, yellow button-down shirt pushes a waist-high tool cart into the hallway. His lived-in sneakers shuffle eagerly forward as he reaches for the rubber bulb of the bicycle horn mounted on his cart. When its sudden staccato blast echoes down the corridors, heads poke out of doorways, and faces light up at the sight of Albert Lexie, a shoe shiner.

Every Tuesday and Thursday, Lexie, 63, awakens at 5 a.m. and catches two buses from his hometown of Monessen to Children's Hospital. He has been shining shoes here since 1981. (His initial price was $2 a pair; now it's $3.) Without fail, he donates all of his tips to the Free Care Fund, a charity that ensures all pediatric patients receive medical care regardless of their ability to pay. (Lexie started saving tips in the hopes that he could make a big gift and meet the late news anchor Patti Burns, who hosted the KDKA telethon for Children's. More than 20 years after he met Burns, he keeps donating.) So far, he has given almost $100,000.

Staff members from the pediatric surgery department greet Lexie warmly as his cart, a gift from the hospital's staff last year, arrives at their door. Many hand over bags of shoes from family members. Lexie pushes his cart to the back of the office, where he finds a seat, unpacks a blue gym bag full of supplies, and lines up the shoes. Barefoot employees gather around like children at an ice cream truck. Someone puts a fresh bagel and cup of coffee on the cart for Lexie. He's full of childlike joy, with a sizable grin and large spectacles pressed tightly against his head.

"He's the only one I've ever known who could get all that salt off my shoes," notes Aileen Sanders, business manager for pediatric surgery.

Lexie buffs a pair of black flats that belong to Sanders while empathizing with her, saying, "You've got to work harder now, since you've got a new daughter now."

Later, as he slips one hand inside a black wing tip, he says, "This makes me very happy to see lots of nice people, lots of nice customers." He turns the shoe from side to side, quickly rubbing the surface with saddle soap. "Shoes got to take a bath, just like people got to take a bath," he says without taking his eyes off the shoe.

Although his daily average is 15 pairs—a day's earnings of just $45—Lexie donates his tips not just from Children's, but also from days shining shoes downtown and in the business districts of the Mon Valley. He puts out cans for donations in area businesses as well.

Sanders checks his coffee to make sure it hasn't gotten cold. She says that Lexie demonstrates that "you don't have to have a lot of money to give a lot of money." Today he charges just $2 per pair of shoes—a special that he offers annually the week before his birthday. Despite the reduced price, he will still eagerly donate every tip. ■



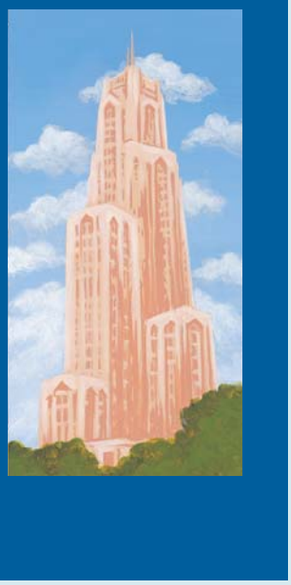
Lexie's tips help sick children.

BOOSTER SHOTS

Back when cataract surgeries weren't so commonplace, ophthalmologist **Norman Gardner Mathieson** (MD '34) met a wealthy industrialist on a fishing trip to Mackinac Island, Mich. When he heard that the man's mother was nearly blind, Mathieson offered to evaluate her for surgery. He successfully operated on both of her eyes, and though the son offered to pay a great deal, Mathieson charged his usual $300 per eye. Decades later, the doctor learned that this woman had left him and his wife 600 shares of stock in a Pittsburgh bank. Over the years, the stock split and resplit into some 22,000 shares. After the Mathiesons passed away not long ago, the School of Medicine received what is believed to be the largest single gift ever from an alumnus: $1.77 million with which to establish the Dr. and Mrs. N. Gardner Mathieson Scholarship Fund.

Broach the subject of medical school tuition, and Senior Vice Chancellor and Dean **Arthur S. Levine** will not hesitate to reveal what he refers to as his "socialist tendencies"—that is, his belief that medical school should be free and that doctors should repay their debt to society through a period of public service. He's not holding his breath waiting for that to happen. In a demonstration of how critical scholarships are to recruiting top students, Levine has announced that his office will redirect some funds from other pressing needs, such as faculty recruitment, in order to double its contribution to student scholarships, bringing its total commitment to approximately $6 million. Still, approximately 80 percent of Pitt med students will finance the bulk of their own educations. —*CS*

FOR INFORMATION ON SCHOLARSHIP GIVING:
1-877-MED-ALUM or mhsf@ia.pitt.edu



CLASS NOTES

'40s

In 1983, **William Donaldson Jr.** (MD '43, Orthopaedic Surgery Resident '46–'49, Pediatric Orthopaedic Surgery Resident '49–'50) trekked through Tibet to reach Mt. Everest with the first American expedition to reach the peak via the east face. Donaldson, an orthopaedic surgeon, former medical director of Children's Hospital of Pittsburgh, and a Distinguished Clinical Professor in the School of Medicine, monitored the oxygen tanks for the climbers at base camp. But Donaldson's fondest doctoring memories are closer to sea level. He established the multidisciplinary clinic at Children's to treat spina bifida. Donaldson started the clinic after becoming frustrated that children with spina bifida were institutionalized instead of being provided with the care they needed to live a more normal life. In the clinic, a social worker, urologist, neurosurgeon, pediatrician, and orthopaedic surgeon worked together to deal with the problems associated with the disease. Donaldson is a member of the School of Medicine's admissions committee. His son, William Donaldson III, is a Pitt professor specializing in spinal disorders.

We already knew **Bernard Fisher** was in elite company. Fisher (MD '43), a Distinguished Service Professor at Pitt and founding member and former chair of the National Surgical Adjuvant Breast and Bowel Project, is referred to as the person who has done the most to improve the lives of women with breast cancer. Now he can count himself in a class that includes Benjamin Franklin, John F. Kennedy, Willie Mays, and Tom Wolfe, to name only a few. At the 303rd Yale University commencement, the institution awarded Fisher an honorary degree (Doctor of Medical Sciences). A few weeks earlier, Memorial Sloan-Kettering Cancer Center gave him the C. Chester Stock Award for "distinguished achievement in biomedical research." Fisher continues his research on breast cancer; he recently published an article in *Lancet* and has one forthcoming in the *Journal of the National Cancer Institute*.

'60s

Psychiatrist **Philip Sandler** (MD '67) says that he loves working "with and for the patient," but recent experience tells him he can't take that for granted. By the time he relocated to the Boston area in 1990, Sandler had worked for a U.S. Naval Medical Center, directed a hospital psychiatry department, and been in private practice. He thought it would be a good experience to work for one of the HMOs that were coming into favor. He saw it as a ready-made practice that would provide him with patients. Plus, he figured that working for the HMO would be easier than asking it for pre-authorizations as a private practitioner. When the HMO started losing money in the late '90s, he says, care suffered. Sandler found that 15 minutes of personal contact per patient was unfulfilling—it only left him enough time to prescribe medication. He left the job in 2001 and worked briefly in his son's real estate business. Although he liked working with his son, he left in 2002 to take what he calls his "dream job" at Boston University Student Health Service. He enjoys the personal interaction with diverse students and their families so much that he plans to postpone his retirement. "It's great to work for the patient again," he says.

In 1981, **Munci Kalayoglu** (Pediatric Surgery Resident '68–'69, Chief Resident for Pediatric Surgery and Urology '69–'70, Research Resident of Pediatric Surgery '70–'71) watched Thomas Starzl perform a liver transplant on a 14-year-old boy with Wilson's Disease—a disorder that causes excess copper to be stored in the liver and brain. Although the body needs copper and absorbs it from food, the improper retention of the nutrient can cause tissue damage and death. After witnessing the young patient's full recovery, Kalayoglu went home and announced to his wife that he was going to be a liver surgeon. In 1987, as associate professor of surgery and pediatrics at the University of Wisconsin School of Medicine in Madison, he performed one of the first extended preservation liver transplants, using a solution he helped develop. The solution can extend the life of a liver outside the body for nearly 24 hours. Most extended preservation liver transplants performed today use this "Wisconsin solution." Lately, he has been dividing adult livers in half to transplant them into two different people, where the organ will regenerate to full size. Split-liver procedures are a promising way to mitigate the liver shortage, he says.

'70s

When a pregnant woman suffers an eclamptic seizure in some parts of Afghanistan, a mullah will beat her to expel the demon, says **Sally Osborne** (MD '76). And in hospitals, patients wait for transfusions while families buy blood from the bazaar. Osborne recalls that in medical school, the late Ken Rogers taught her that a site visit was absolutely necessary to understand community hospitals and clinics. Indeed, before learning such things firsthand, Osborne would never have anticipated the problems at Rabia Balkhi Women's Hospital in Kabul, where she trained doctors for three months in 2003. The U.S. Department of Health and Human Services, the Afghanistan Ministry of Health, and the nonprofit group International Medical Corps organized that mission. A colleague advised Osborne not to eat anything before arriving at the hospital, and with good reason: Putrefying medical waste was piled outside the front door because the incinerator was broken. The stench was nauseating. With shortages of basic supplies like bleach, the underpaid, undertrained, overstretched staff was profoundly discouraged. Some doctors often skipped out early, supplementing their income through private practice. On one occasion, the hospital staff failed to inform a patient's family that the patient had died. When the family found out, they threatened the hospital with guns in tote. Osborne persuaded the staff to take record keeping seriously, to work on communication, and, she believes, to care again. She says she feels a spiritual calling to humanitarian work ever since she retired from her ob/gyn practice in 1999. As a board member of the Foundation for International Missions, she is now involved with planning a small medical/dental clinic in a rural mountain area of Honduras.

'80s

When **Karen Kotloff** (Pediatrics Resident '80–'83) arrived in Pittsburgh, she was interested in child psychiatry, but she found that she loved pediatrics so much that she decided to skip psychiatry. Now, as a professor of pediatrics and medicine at the University of Maryland School of Medicine, she spends

several weeks a year running vaccine trials in Mali to help stop the spread of preventable disease. Kotloff primarily trains the residents of this landlocked West African nation to conduct the trials and teaches them the clinical and ethical guidelines involved in the process. Through this collaborative relationship between the university and the Malian Ministry of Health, she also works with Malian researchers to design studies of the epidemiology of infantile measles and diarrheal diseases. At Maryland's Center for Vaccine Development, Kotloff focuses on bacteria that cause diarrheal diseases such as *Shigella, Helicobacter,* and *Streptococcus* (Group A)—conditions that most often affect children.

While **John M. Roberts** (Research Fellow '81–'82, Orthopaedic Resident '82–'85) was working in Pittsburgh, he became enamored of vintage grand prix racing. Soon he was spending all his free weekends racing. Now living in Cincinnati, he says he gladly gave up this pastime when his wife asked if he could put the hobby aside to spend more time with his four daughters. As they grew up and wanted to spend more time on their own than with their father, Roberts was without a hobby to occupy his free time. So he started writing. First came all the bedtime stories he had made up for his daughters, published in *Walloon Tales* (inspired by their vacations at Walloon Lake, Mich.). His second book, *Carrington House,* was released last year. The mystery novel describes an act of revenge at a private boarding school that draws the attention of the nation's top pathologists. As Roberts writes his next book, a sci-fi thriller, he'll continue in his private practice, which focuses on spinal deformities. He and his partner will soon be performing disc replacement surgeries with a new product made by DePuy Orthopedics.

The last time **Robert Brenner** (MD '87) was in Pittsburgh, he got a splinter. The splinter was so deeply embedded in his finger he had to go to the ED at UPMC Presbyterian. He was surprised to see all the changes that have been made at the hospital since he was a student. As the director of business development and chair of family medicine for Mountainside Hospital in Montclair, N.J., he paid careful attention to the newest details in the ED to share with his colleagues. Since starting this position in March, Brenner has helped to develop a sports medicine center and melanoma center and rebuild a primary care network. Brenner, who spent most of his med school years soaking up wisdom from surgeons Thomas Starzl, Charles Watson, and Bartley Griffith before suddenly switching to family medicine, still holds clinic a few times a week. He says he's unable to give up medicine completely for his administrative duties.

'90s

When he was a young child in Harrisburg, **Daniel Edmundowicz** (Cardiovascular Fellow '93–'96) would often accompany his father, a cardiologist, on hospital rounds. Sometimes, they even went on house calls. The boy would sit and talk with his father's patients, or silently keep them company if they preferred. Years later, in med school, he was determined to explore his interests in neurology and oncology, to venture outside of the world of cardiology that was his dad's. But the exposure to cardiology during internal medicine training in his senior year brought him back to that subspecialty. Cardiovascular disease is, for the most part, very preventable, he says, so cardiology provides him the opportunity to educate his patients ("I love to teach," says the Pitt associate professor of medicine), work with them to improve their health, and witness positive changes like lowered blood pressure and cholesterol levels. During his fellowship at Pitt, Edmundowicz met Lewis Kuller, professor of epidemiology, who further piqued his interest in understanding and preventing cardiovascular disease. Now Edmundowicz is the director of preventive cardiology for the UPMC Cardiovascular Institute, where he directs the lipid clinic and the electron beam tomography (EBT) program. Pitt researchers were among the first to find that HIV patients have a high prevalence of coronary artery calcification, probably because their anti-viral medications increase cholesterol levels. Armed with this knowledge, many HIV patients now visit the lipid clinic for preventive treatment. On rounds, Edmundowicz has been known to cheer up his patients by popping in with a few of his four children in tow. "That's what I learned from my dad," he says, "to care for the whole individual and to remember that good mental spirits can help lead to better health."



The Hippocratean, 1999

Amy Juraszek (MD '96, Pediatrics Resident '96–'99) always thought the faculty and staff at Pitt made teaching a priority. She tries to do the same as a pathology instructor in the Harvard Medical School and medical director of the Cardiac Registry at Children's Hospital Boston. The registry's use of imaging techniques has been helpful to Juraszek in her efforts to improve the curriculum for teaching cardiac anatomy and pathology. Yet, as an instructor to cardiology fellows and a lecturer at Harvard Medical School, she prefers going back to basics—using real pediatric heart specimens as teaching aids, rather than high-tech three-dimensional imaging. Juraszek also collaborates on research into GATA-4, a transcription factor involved in heart development.

Aaron Bornstein (MD '99) only applied to Pitt's School of Medicine to round out his application fees to an even $200. But after an interview, Bornstein fell in love with Pitt and moved it up to his first-choice school. Now working as a consultant pediatrician at Masterton Hospital in New Zealand, Bornstein has found that helping families that are struggling to obtain medical resources and care can be the most fulfilling aspect of his job.

'00s

Lily Im (MD '00, Ophthalmology Resident '01–'04) experiments with view and perspective when she does macrophotography, which is essentially taking big pictures of small things. "I like viewing objects, especially flowers, up close, because there's often a very complex microenvironment." As a brand-new clinical associate and glaucoma fellow at Duke University, Im is not just looking at flowers up close. She is examining glaucoma—a disease that has long been studied but is still shrouded in mystery. She, like other ophthalmologists, wonders if there is a connection between glaucoma and Alzheimer's, and how large a role intraocular pressure plays in the resulting damage to the optic nerve. (It was once assumed that this pressure was the cause, but new research shows it is only a contributor.) — *MH, MD, CB*

Calling All Kudos

"Everyone has talent at 25. The difficult thing is to have it at 50," said Edward Degas. Who among your peers has stood the test of time? The Medical Alumni Association is seeking nominations of outstanding alumni for the Hench and McEllroy Awards.

The Hench Distinguished Alumnus Award is presented annually to a graduate of the School of Medicine. The McEllroy Award recognizes outstanding doctors who undertook residency training at Pitt but received their MDs elsewhere.

Please send CVs and/or letters of nomination to:
University of Pittsburgh
Medical Alumni Association
M-200K Scaife Hall
Pittsburgh, PA 15261
Tel: 412-648-9090
Fax: 412-648-9500
E-mail: medalum@medschool.pitt.edu

THE WAY WE ARE

CLASS OF '94



The Class of '94 gathered for their 10th: (back row, from left) D. Dean, S. Beardsley, D. Vangura, W. Alarcon; (middle row) D. Warren, D. Goldman, J. Chen, J. Hofmeister, D. Kim; (front) A. Lim, A. Nowalk, M. Hofmeister, K. Ciccarelli. L. Le

After 10 years, most attending the Class of '94 reunion in May looked about the same, though **John Wilkinson** says he got more than a few odd looks because of his shaved head, goatee, and earrings. Wilkinson is a tactical physician for the police Emergency Response/ SWAT team in Gastonia, N.C. His team sometimes trains with the Army Special Forces Advanced Urban Combat School, acting out and responding to realistic military scenarios on a large scale. Sometimes one group gets to play the bad guys.

He and his wife, **Michelle Wilkinson** (also MD '94), did an emergency medicine rotation at the Royal Victoria Hospital in Belfast, in Northern Ireland during their final year in medical school. They were a bit apprehensive at first, because the police carried machine guns and many victims of political violence came into the ER. When her husband returned to Ireland in 1996 for a rotation, Michelle Wilkinson stayed behind with their 1-year-old. She has been in private family practice for seven years, and she loves delivering full-scope care—that is, everything she was trained to do, including pediatrics and obstetrics. Her patients include families that span four generations and one that spans five.

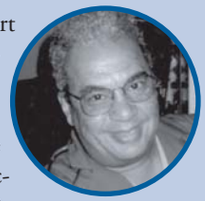


Vangura

Dave Vangura strongly considered pediatrics because he so admired Kenneth Schuit, Pitt pediatrician and infectious disease specialist. However, Vangura now happily works as an army anesthesiologist. Vangura has been in the military since his internship at Tripler Army Medical Center (TAMC) in Honolulu, and he hasn't stopped traveling since. He was sent to a small town in Germany as a flight surgeon and was deployed to Bosnia for one winter, where he lived and worked in heated tents and ran a regimental aid station with one other doctor and six medics. After an anesthesiology residency at Walter Reed Army Medical Center in Washington, D.C., Vangura was sent to Wuerzburg, Germany; there he served as a staff anesthesiologist from 2000 to 2003. From Wuerzburg, he has been deployed to the Republic of Georgia and briefly to Kosovo. He met his wife, Karin, also an anesthesiologist, at a salsa dance lesson in Wuerzburg. If he could go back in time to when he began medical school, Vangura says he would take the army scholarships again without second thoughts. When his military commitment ends soon, however, after a total of 12 years, he plans to leave the army.

David Kim is enjoying his role as a hands-on teacher of med students and residents. He's currently an assistant professor of anesthesiology at Temple University. He finds it especially gratifying to watch his students as they become more comfortable with patients. He recalls recently teaching a student how to give an epidural to a pregnant woman. Upon seeing the patient begin to feel better, the student turned to Kim and said, "So this is why you like anesthesia." Exactly. And it's a pleasure to teach, says Kim. —*Corey Ballantyne*

ROBERT G. KISNER
JUNE 15, 1940–MARCH 29, 2004



Kisner

At one time in the 1970s, Robert Kisner was the only private practice ob/gyn at Magee Womens Hospital who would deliver babies for women on the state's medical assistance health insurance program, says his practice partner, Morris Turner (MD '73). Kisner (Res '73) was reimbursed only $90 (private insurers paid $1,000 or more), but he thought it was important that poor women have an alternative to delivery by residents in training at a hospital clinic. Throughout his career, Kisner, who died suddenly this year at age 63, delivered care regardless of a patient's ability to pay.

Kisner was raised by his mother in Pittsburgh's Hill District, where poverty was endemic and women, in particular, struggled to provide for themselves and their children. He left home in 1959 for the educational opportunities offered by the South's historically Black colleges. He was a star swimmer at Morgan State University in Baltimore, and, in 1969, graduated from Meharry Medical College in Nashville, Tenn. He returned to Pittsburgh that year to become one of the first African American physicians trained at Magee Womens Hospital. As a student and ob/gyn resident, he saw women suffer and even die of complications from illegal abortions. In 1973, following the U.S. Supreme Court decision legalizing abortion, he was one of the first physicians in the city to perform the procedure. For many years, he endured angry protests outside his East Liberty practice and even his home. Turner says that their shared practice was targeted because he and Kisner refused to hide the fact that they performed abortions, believing that in a climate of fear, they had a responsibility to assert that women had a right to safe and complete medical care.

For many years, Turner and Kisner also set up health clinics in Monongahela Valley towns where the families of unemployed steelworkers had lost their health insurance and access to good care. Kisner was also noted for being one of the first physicians in Pittsburgh to make full use of nurse practitioners and physician's assistants to significantly increase the number of patients he could treat.

—*Chuck Staresinic*

IN MEMORIAM

'30s

A. NATHAN ALPERN
(MD '38)
SEPTEMBER 11, 2004

'40s

DAVID A. HUOT
(MD '45)
SEPTEMBER 5, 2004

HARRY R. ZELLER
(MD '47)
SEPTEMBER 22, 2004

RANDALL KOLB: IN SERVICE

BY MEGHAN HOLOHAN



COURTESY COTTER

Kolb with children in Honduras.

Tears run down Kristen Cotter's face as she stands in a Scaife Hall bathroom. As a first-year medical student, she has been upset a lot. Starting school, she'd already felt behind because she majored in sociology and writing and took three years off after college. She's not doing well in her classes. A few months ago, she gave herself an ultimatum: *If I don't get a good preceptor, I'm going to quit.*

Now she's in the bathroom crying. She and her preceptor didn't hit it off. She'd spent the previous three years working in public health in Indonesia and then decided to become a doctor to alleviate suffering. She wanted a preceptor who could inspire her and help her play a part in the human side of medicine—help her see past the biochem and anatomy that, to her, seemed so far away from helping others.

She thinks that maybe she can arrange for a new preceptor herself. So she calls Randall Kolb (MD '82), who doesn't know her from Eve, though they both attend the Pittsburgh Mennonite Church. She nervously tells him how she is so discouraged in med school that she wants to quit.

Five years later, Cotter (who took a year off to earn a Master of Public Health degree from Tulane University) is an ob/gyn resident at Women & Infants Hospital of Rhode Island in Providence.

Having the opportunity to observe Kolb made all the difference. She recalls the young woman who'd never had a pelvic exam: "He just made sure that what he was doing was okay. She felt extremely embarrassed and uncomfortable, and he met her where she was."

And Cotter remembers how Kolb interacted with a schizophrenic patient: He asked what outlets she had for her artistic side.

In Kolb, Cotter (MD '04) found a preceptor who was the kind of doctor she wanted to be. He's an inspiration to others, too. This past January, the American Institute for Public Service recognized Kolb, director of the Family Health Center at UPMC Shadyside and a clinical assistant professor of family medicine, with a Jefferson Award for Public Service.

The reserved Kolb will pause before making a remark, as though he's taking time to consider a problem. He prefers to hand the reins of their lives back to patients. "What would you like to do?" he'll ask an addict, rather than lecturing her about how she needs to quit using drugs.

He often wonders how he can best serve. He works at Bethlehem Haven, a shelter for homeless women, and with Pittsburgh's Health Care for the Homeless program. Kolb helped obtain a grant for an x-ray machine that the Allegheny County Health Department uses to determine whether people who are homeless have tuberculosis (so far not one has had the active form of the disease in the county). And twice a year, he does work in Honduras.

Kolb first visited that country in 1999, in the wake of Hurricane Mitch. After that, Kolb joined William Markle, assistant professor of family medicine at Pitt, and Mark Meyer, a family practice physician, as they were establishing a global health elective. To fulfill the elective, students help staff a clinic in rural Honduras. Cotter has worked there as well.

"You get to see a lot of patients because you don't have to do a lot of paperwork, and when you are there, there is nothing else to do," says Kolb. "You get up and eat breakfast, and you see patients, and at night, you talk about patients, and you play cards and go to sleep. It's a very focused experience. It also gives a chance to explore, 'What does it mean to be a doctor?'"

On the pragmatic side, that means, for Kolb, using his own resources as a diagnostician rather than relying on tests. Yet more profoundly for him, being a doctor is about more than just treating a medical condition—it's about treating the human condition. ■

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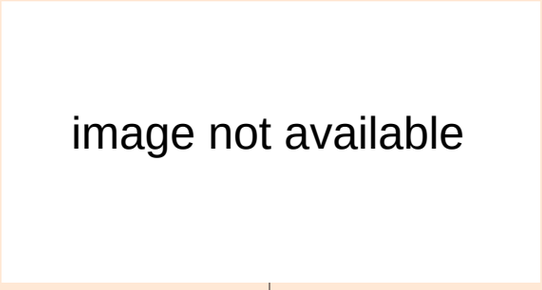
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SICK, SICKE, [SIC]



What follows is from **The Ladies Dispensatory,** *a guide to self-help medications and herbal remedies, first published in London in 1652. It was republished in 2003 by Taylor and Francis and edited by Jonathon Erlen, history of medicine librarian for Pitt's Health Sciences Libary System, and Carey Balaban, Pitt professor of otolaryngology.*

Against the stinging and biting of venomous Beasts.

Chicken braines taken in wine.

Caterpillars applyed with oyle.

Bloud of sea Tortoise drunk with Cummin, and the curd of a Hare.

Bastard wild Poppy taken in wine.

Strong brine dropped into the wound.

Against the biting of Vipers.

Chickens cleft alive, and applyed on the wound.

The Patients own urine drunk.

Garlick taken in wine, or applied.

Against the biting of Serpents and Aspes.

River Crabbs bruised, and drunk with Asses milk.

Powder of Weesils salted, and dryed in the shadow, the weight of two drams taken in wine.

Froggs boyled in oyle, eaten with salt.

A Bores liver dryed, and taken in wine.

Incision made in the Patients head unto the bone, Euphorbium put therein, and the wound re-closed.

Against the biting of Serpents called Emourrous.

Pure wine drunk abundantly.

Against the stinging of Waspes, and Bees.

Decoction of marsh Mallowes drunk in water and vinegar.

Against the biting of shrew Mice.

The shrew Mice themselves cut in peeces, and applyed on the wound.

Wild Time taken in wine.

Against the biting of mad Dogs.

Blood of a dog drunk.

Urine of a dog drunk.

Stinking Hore-hound applied with salt.

Against the biting of Weesils.

Rocket eaten, but you must drinke good wine presently after.

Against the stinging of Scorpions.

Scorpions bruised, and applyed, or rosted and eaten.

Lizards opened, and applyed take away the paine.

Mice opened, and applyed.

Against the Venomes and Poysons of Toades and greene Froggs.

Wine abundantly drunke, and vomited.

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CALENDAR

OF SPECIAL INTEREST TO ALUMNI AND FRIENDS

SCHOOL OF MEDICINE RECEPTION
NOVEMBER 7
AAMC Annual Meeting
Boston Marriott Copley Place
Simmons Room
Boston
5:30 p.m.
For information:
Office of the Vice Dean
412-648-9000
vicedeanstaff@medschool.pitt.edu

C.F. REYNOLDS MEDICAL HISTORY SOCIETY SERIES
JANUARY 27
"Neck Dissection: An Operation in Evolution"
Eugene Myers, MD, Speaker
FEBRUARY 17
"Biological and Chemical Warfare: An Historical Perspective"
Douglas Bacon, MD, Speaker
All lectures are at 6 p.m.
Scaife Hall, Lecture Room 5
For information:
Jonathon Erlen
412-648-8927
erlen@pitt.edu

BAHNSON LECTURE
MARCH 2
G. Alexander Patterson, MD
Speaker
Scaife Hall, Lecture Room 5
For information:
Kathleen Haupt
412-647-5314
www.surgery.upmc.edu

BLACK BAG BALL
APRIL 22
Omni William Penn
Pittsburgh
For information:
Medical Alumni Association
412-648-9090 or 1-877-MED-ALUM
medalum@medschool.pitt.edu

PITT MED GOLF OUTING
APRIL 23
Quicksilver Golf Club
Midway, Pa.
8:30 a.m.
For information:
Ronald Trible
412-648-9090
rptst7@pitt.edu
www.pittmedgolfouting.org

MINORITY ALUMNI WEEKEND
MAY 13–15
Pittsburgh
For information:
Office of Student Affairs/
Diversity Programs
412-648-8987
minorityaffairs@medschool.pitt.edu

ALUMNI WEEKEND 2005
MAY 20–23
Classes celebrating:
- 1940
- 1945
- 1950
- 1955
- 1965
- 1970
- 1975
- 1980
- 1985
- 1990
- 1995

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TO FIND OUT WHAT ELSE IS HAPPENING AT THE MEDICAL SCHOOL, GO TO www.health.pitt.edu



SHINE YOUR SHOES

and make sure they still fit before you step out for the next Medical Alumni Weekend.

Reunite with your classmates during the Dean's Breakfast, Saturday night dinner, and the latest incarnation of Scope and Scalpel. You'll also want to meet the newest Pitt med grads at the Senior Class Luncheon.

To find out if your class is celebrating this year, check the calendar on the back of this page.

Medical Alumni Weekend
May 20–23
Sheraton Station Square, Pittsburgh

For more information:
1-877-MED-ALUM
medalum@medschool.pitt.edu
www.medschool.pitt.edu/alumni

GETTY

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SCHOOL OF MEDICINE
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CHANGE SERVICE REQUESTED