UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | JANUARY 2001

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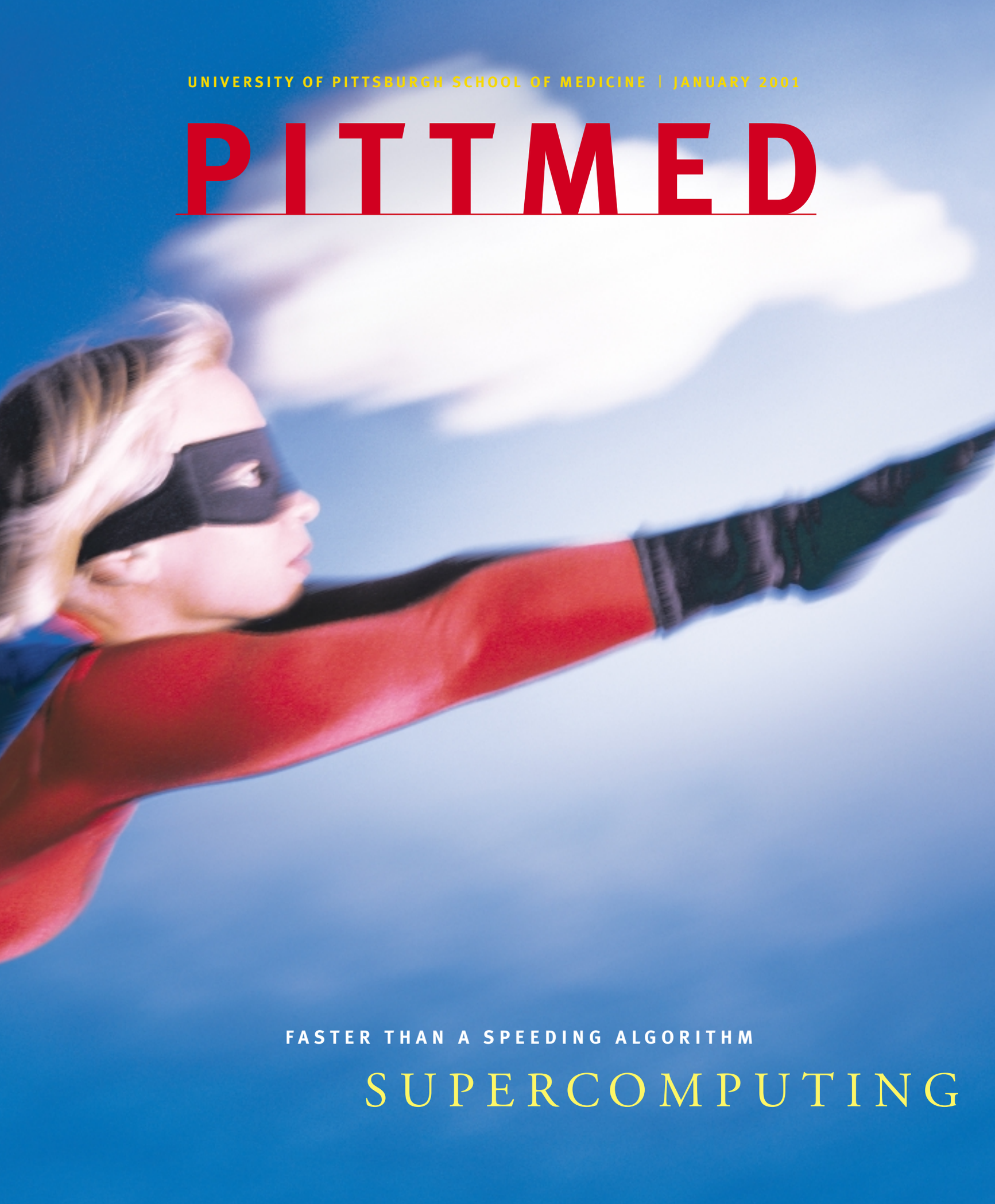

FASTER THAN A SPEEDING ALGORITHM

SUPERCOMPUTING

PITT MED
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2001

A GOLDEN MOMENT

Here at *Pitt Med* we were pleased to learn that the magazine has won another Council for the Advancement and Support of Education (CASE) Gold Medal, this time for our district (which covers the Mid Atlantic, meaning most of the East Coast as well as Quebec and Ontario). *Pitt Med* took CASE's top honor for general interest magazines against plenty of well-established and respected competition. We were pleasantly surprised.

RAINDROPS ON ROSES AND GASTRIC ANALYSIS

Regarding your "Last Call" photograph in *Pitt Med*, October 2000 [above].

What a surprise to turn to your last page and see my med school classmates doing our own gastric analyses in organic chemistry. That would be the fall semester of 1952 (Class of 1956).

From left to right are Rudy Janosko, Joe Bayer, Fred Klein, and my roommate, Gerald Johnston. Back in those days, we all wore ties every day.

It spurred me to call my classmates and talk about the picture, reliving old, old times.

Thanks for the picture.

Joe Karcher, MD '56
Hemet, California

The photo was taken (I think) in the fall of 1953—during physiology class and shows four of my classmates being intubated to recover gastric juices. Rudy Janosko is on the left and Gerry Johnston is on the right. I knew them well because, together with Joe Karcher, we shared a cadaver during our freshman year, 1952.

John L. (Jack) Humphreys, MD '56
Atlanta, Georgia

We received many notes about the gastric analysis photo. There was some confusion about the year and whether that's Fred Klein or Charles Pifer third from the left. Yet, it must have been a good class. Bernard Miklos, MD '56, says that he remembers that day as though it were yesterday. And Mervin Stewart, MD '53, recalls taking that photo and many others for the yearbook—including our back cover photo in this issue.

MENTEN COMMANDED RESPECT

I enjoyed your article on Maud Leonora Menten [October 2000]. Those of us who sat under her teaching more than 50 years ago are not likely to forget her or the excellence of her work. You may be sure that we addressed her as Doctor Menten!

I was told at the time that Dr. Menten had a particular dislike for driving through tunnels.

(I believe that is Dr. Lacey, who headed the microbiology department, in the 1950 photo of the gathering honoring Dr. Menten's retirement from Pitt.)

Robert F. Kleinschmidt, MD '45
Pittsburgh, Pennsylvania

Your interesting piece on Maud Menten ends with the question "who?" There are some people who may know the answer. George Michalopoulos, MD, PhD, chair of pathology, for example, holds the Menten Chair in Experimental Pathology, and the Department of Pathology hosts an annual Menten Lecture in Experimental Pathology. Dr. Menten was a staff pathologist at Children's Hospital, and since Dr. Menten's induction into the Canadian Medical Hall of Fame in 1998, the award is on display in the Menten Conference Room. Her presence is still felt.

Ron Jaffe, MD
Department of Pathology

The article on Maud L. Menten, MD, PhD, was a very good one and gave credit to an extraordinary person. I would like to amplify on the initiative by the Department of Pathology to honor her.

In 1988, the department raised funds to endow a chair in her honor: the Maud L. Menten Professor of Experimental Pathology. I was the first to hold this chair, and George Michalopoulos, MD, PhD, a distinguished experimental pathologist and the chair of the Department of Pathology, is the second. In addition, the department has endowed an annual lectureship in her honor. It also secured a full-length portrait of Dr. Menten, painted by one of her artist colleagues; the portrait now hangs in the school's main auditorium.

These acts of recognition preserve the memory of a unique and versatile person—though belatedly. Such recognition of an outstanding member of the University community serves not only to honor the person involved but also to provide inspiration for the University's future development.

Thomas J. Gill III, MD
Maud L. Menten Professor of Experimental Pathology Emeritus
Department of Pathology

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At first, not everybody thought a physician was the right person to run Purdue University, but Pitt alum Steven Beering changed their minds. His secret may be leading with a very, very big picture.
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Ed Jackson and Joseph Carcillo didn't get into research for the money; yet as they attempt to prevent acute renal failure, they may want to get a broker.
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Pitt's Herb Needleman changed the way we think about children's exposure to lead at levels once considered subclinical. Now he warns that exposure can contribute to delinquency as well as lower IQs.
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CONTRIBUTORS

DOTTIE HORN — ["Ka-pow!" and other contributions] Dottie Horn didn't move to Pittsburgh from North Carolina just for the ice-skating lessons. Our new associate editor and official Southerner has braved a wintery Fifth Avenue to cover news about all things *Pitt Med*ish, but especially stories on students and the curriculum. The magazine already has benefited from her talents honed on the University of North Carolina at Chapel Hill's research magazine and from other writerly forays.

MIKE MCQUAIDE — ["His Personal Cosmos: Indiana"] is an illustrator for advertising agencies in Pittsburgh and elsewhere. The graduate of the Art Institute of Pittsburgh lives in the South Hills and has three children ranging in age from 14 to 20. His eldest son is a junior at, excuse the expression, Penn State.

COVER

Okay, maybe Pitt crusaders prefer lab coats to capes, but their research is definitely super. (Photo by Craig Thompson)

PITTMED

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JULIA MAROUS STRAUT

In a busy hospital corridor, the father of a young girl with cancer asks his daughter's physician to tell him more about her condition. The doctor responds with data on the girl's blood tests and drug regimen. This is not the information the father is searching for, however. What this man really wants, though it may not be apparent even to him, is to sit down and discuss his own sense of guilt and complicity in his daughter's illness. Doctors have told him his daughter is dying. He needs an answer to a question that will take some courage to articulate: *Is there anything I could have done differently that would have saved her?*

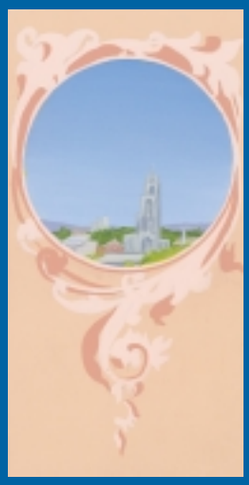
During my years at the National Cancer Institute, I became aware of such scenarios playing themselves out again and again. Sometimes physicians, typically newly arrived oncology fellows, would sense a parent's need to talk but would not allow themselves to engage in "real life" discussions. They were uncomfortable taking on such counseling, or claimed it would eat into their time. Other oncology fellows grappled with displaced anger, frustration consequent to an inability to fulfill a "hero-rescuer" role, and the like. My colleagues and I soon recognized that unless these issues were brought to light, the clinical setting would become a tangle of mis- and missed communications.

What patients and their families go through as they deal with life-threatening illness offers a magnification of what others may experience. A patient might think, for example, that a pain in her chest means she is having a heart attack when really she is experiencing indigestion. Our students must learn to, as appropriate, calm suspicion and anxiety about dreaded illnesses. And in cases of life-threatening conditions, they must confront the stark reality of unfairness, recognizing that the world is sometimes unreasonable and unresponsive despite our very best efforts and wishes. No matter how much we may want to tell that father his little girl will be okay, we can't, and we need to recognize the scope of that hurt in the family and often the community.

Even in the most tragic of circumstances, the doctor-patient relationship can be uniquely rewarding to both. It is unlikely to be so, however, if physicians do not understand the many social and psychological dynamics at work in their interactions with their patients and patients' families. The late Dr. Leo Criep, a prominent allergist/immunologist and Pitt professor, was well aware of the complexities of this relationship. Dr. Criep passionately asserted that during this age of tremendous biomedical research promise, scientific acumen was no substitute for compassion, insight, and understanding. In his honor, his family has worked with the School of Medicine to establish what is believed to be the nation's first endowed chair focused on the dynamics and philosophy of patient care. After an extensive national search, Robert M. Arnold, professor of medicine, has been chosen to serve as the chair's first incumbent (see p. 36). Like Dr. Criep, Dr. Arnold is a clinician, scientist, and teacher; and like Dr. Criep, he is committed to creating the best possible environment for meaningful communications and interactions between doctors and their patients. I've asked him to bring his leadership, creativity, and vision to the school's extensive efforts to promote humanism in medical education and clinical research.

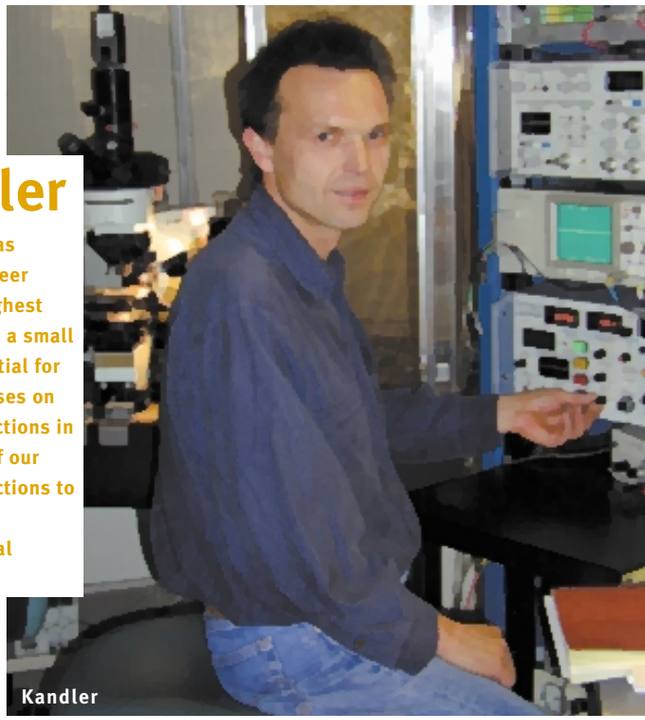
Art Levine

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



Devoted to noteworthy happenings at the medical school. . . Also, to stay abreast of Pitt health sciences news, including info on faculty and research, see http://www.health.pitt.edu

White House Salutes Kandler



Kandler

Karl Kandler, assistant professor in the Department of Neurobiology, was invited to the White House in October to accept a Presidential Early Career Award for Scientists and Engineers (PECASE), considered one of the highest honors the US government bestows on researchers. The award identifies a small cadre of researchers who, early in their careers, show exceptional potential for leadership at the frontiers of scientific knowledge. Kandler's work focuses on the development and function of what are known as "inhibitory" connections in the brain. Little is known about these connections—yet probably half of our neuronal connections are inhibitory and our brains rely on these connections to process visual, auditory, and other information they receive.

Kandler was one of only 12 researchers nominated by the National Institutes of Health for the PECASE. *—EL*

FOR MORE INFORMATION: http://www.neurobio.pitt.edu/faculty/kandler.htm

FOOTNOTE

Maybe the Nobel committee should check in with Pitt first. Six of the Nobel Prize for Medicine winners were first awarded the School of Medicine's Dickson Prize, including this year's Nobel corecipients, Paul Greengard and Eric Kandel (lauded with Arvid Carlsson for their work on signal transduction in the nervous system).

PSYCH!

No psychiatry department in the country comes close to Pitt's when the subject is National Institutes of Health (NIH) funding. By receiving $59 million last year, Pitt's department was privy to nearly double the funding of Yale's, whose $32 million placed it second on the list. In fact, more than 10 percent of all NIH money awarded to the country's 87 departments of psychiatry was granted to Pitt researchers. About $30 million of the total came from the National Institute of Mental Health (NIMH), making Pitt the largest single recipient of NIMH funding. *—DH*

FOR MORE INFORMATION: http://www.wpic.pitt.edu

FRANK WALSH

THREE BLIND MICE? TAKE A NUMBER.

Answering questions about gene function was never so easy. Med school researchers wanting mice with customized genes need only look next door, now that Pitt's Transgenic and Chimeric Mouse Facility is up and running. There, a litter of genetically altered pups costs as little as $2,500. Researchers buying similar animals from a biomedical firm could pay tens of thousands of dollars per model. And a primary service of the facility is free, i.e., consultation to help researchers refine their experiments and accomplish their goals. "Making animal models or testing experimental hypotheses using genetically altered mice is a very long, tedious process," says J. Richard Chaillet, associate professor of pediatrics and the facility's scientific director. "It often demands coming to grips with results that don't make sense or experimental procedures that don't work. The intention of having the facility on campus is that we can work almost on a day-to-day basis with people, helping them with every particular step along the way." These services also will make it easier for Pitt nongeneticists to expand their parameters of discovery. ***—DH***

Faculty Snapshots

A LOOK AT SOME OF THE PROJECTS SCHOOL OF MEDICINE FACULTY MEMBERS HAVE TAKEN ON OF LATE:

Premenopausal women setting a date to quit smoking may want to consider their menstrual cycle. Women who quit on days one to 14 following menstruation had less severe symptoms of nicotine withdrawal and depressed mood than women who quit on day 15 or later, according to a study by **Kenneth Perkins**, professor of psychiatry.

Stray microscopic calcium crystals float in the inner ear, interfering with nerve signals, causing benign paroxysmal positional vertigo. The condition was the subject of a review article in the *New England Journal of Medicine* by **Joseph Furman**, professor of otolaryngology, neurology, bioengineering, and physical therapy. "Dizziness has a tremendous impact on the quality of people's lives," says Furman. "There aren't that many conditions in the dizziness world that are as easily treatable as this one." Physicians can often relieve symptoms with a head-tilting procedure. "When it works, it's just magic," says Furman of the treatment, which has a success rate of 90 percent.

Hemifacial spasm, which affects one in 100,000 Americans, causes uncontrollable facial twitching, sometimes so severe that a person cannot read or drive. First-line therapy is botulinum toxin (Botox) injections. However, a study by **Amin Kassam**, assistant professor of neurological surgery and codirector of the Center for Cranial Base Surgery, shows that patients who receive Botox injections prior to decompression surgery actually end up twitching more, 13 months later, than those who don't receive the injections prior to surgery. Kassam also is helping to establish a new Surgical Technologies and Training Center, where surgeons will work with companies such as Olympus and Stricker to develop new surgical equipment. Surgeons also will be trained on the equipment through the center.

Kassam

Since May 1990, 143 patients have received 151 intestinal transplants at UPMC Health System. Even here, one of the world's premier transplant centers, 84 percent of those patients experienced at least one episode of rejection and 22 percent of their transplanted organs failed. A new technique developed by **Kareem Abu-Elmagd**, associate professor of surgery and director of intestinal transplantation, may improve organ acceptance rates. His five patients who received intestines irradiated before transplantation, along with a standard bone marrow transplant, have shown no evidence of rejection for up to four months. *—DH*

Abu-Elmagd

FOOTNOTE

"One of us found anatomy lab so incredibly intriguing that [he/she] threw up the first day."

"It's every week. I just run. There's a trash can right outside the door. I don't make a spectacle of it; and then I just come back in and get down to work."

—Anonymous, MD '04 & Anonymous, MD '04

SCAIFE GRANT FERTILIZES NEURODEGENERATIVE RESEARCH

A $10.8 MILLION GRANT FROM THE SCAIFE FAMILY FOUNDATION AND SCAIFE CHARITABLE FOUNDATION WILL HELP ESTABLISH THE PITTSBURGH INSTITUTE FOR NEURODEGENERATIVE DISEASES.

The institute will bring scientists currently scattered across the campus together in a new facility and build on existing expertise by adding faculty. Construction for the new institute will begin within the next two years.

The simple act of bringing researchers into adjoining laboratories is important, says Michael Zigmond, professor of neurology and codirector of Pitt's National Parkinson's Disease Center of Excellence. "In science, the number of times you bump into people, even on the way to picking up coffee or getting your mail, has a major influence," says Zigmond. "The most important single change that this institute will produce is increasing the frequency of interactions. My experience is that if you put two researchers together for a couple of hours, if they have anything remotely in common, an experiment is going to emerge. That's what we want to foster."

Physicians will treat patients in the institute's clinics and mingle with basic and clinical researchers, learning through casual interactions and formal seminars about research developments and clinical trial opportunities. The goal is to hasten laboratory discoveries and translate them more quickly into better patient care, notes Steven DeKosky, professor and interim chair of the Department of Neurology. "The idea of the lone scientist working in his or her laboratory is, for the most part, an image very much of the past," says DeKosky. *—DH*

Stress Matters

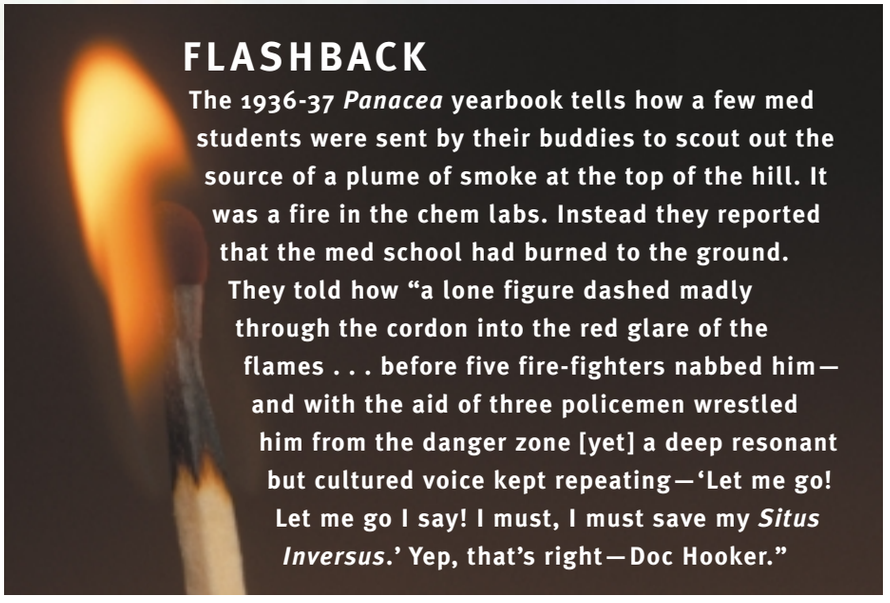
When psychological stress hits, blood hormone levels change, triggering the suppression of the immune system. But what does this mean, say, to a man going through a lengthy and painful divorce? Is he more likely to become sick?

"Stress is a major factor in predisposing individuals to disease development," says Bruce Rabin, professor of pathology. Rabin last year was a coauthor on a review article commissioned by the *Journal of the American Medical Association* focusing on stress-induced immunomodulation.

In one study cited by the coauthors, researchers at the Common Cold Centre in England exposed people to viruses causing upper respiratory tract infections. Subjects who became sick reported more stress-filled lives than those who stayed well.

A few years ago, Rabin and other School of Medicine researchers, in collaboration with Sheldon Cohen at Carnegie Mellon University, repeated the study and determined that chronic stressful events—those lasting a month or longer—increased the risk of developing illness. Chronic social conflicts as well as underemployment and unemployment were deemed especially guilty culprits. Yet people who had social ties in different areas of their lives—at work, at home, and at church, for example—were less likely to become sick.

"If you have a lot of social support and friends, and you're physically fit rather than sedentary, and you're more of an optimist than a pessimist, it's less likely that the stress will have an effect on your health," notes Rabin. *—DH*



FLASHBACK

The 1936-37 *Panacea* yearbook tells how a few med students were sent by their buddies to scout out the source of a plume of smoke at the top of the hill. It was a fire in the chem labs. Instead they reported that the med school had burned to the ground. They told how "a lone figure dashed madly through the cordon into the red glare of the flames . . . before five fire-fighters nabbed him—and with the aid of three policemen wrestled him from the danger zone [yet] a deep resonant but cultured voice kept repeating—'Let me go! Let me go I say! I must, I must save my *Situs Inversus*.' Yep, that's right—Doc Hooker."

IMAGES: EYEWIRE

EYEWIRE

Appointments

As the new codirector of the Brain Tumor Center at the University of Pittsburgh Cancer Institute (UPCI), **Clifford Schold** plans to help enhance the center's visibility and reputation. Schold joined Pitt as a visiting professor of neurology and director of UPCI's Neuro-oncology Program in August, coming from Duke University. He'll also serve as assistant vice chancellor for clinical research. His research into drug therapy for nervous system tumors complements Pitt's strong history in fighting nervous system cancers using radiation therapy and radiosurgery. "Most of us believe there's not going to be one answer to these tumors," says Schold. "It's probably going to take some combination of high dose radiation and chemotherapy, which is why my coming here is a nice match."

Schold

Augustine Choi, a visiting professor of medicine, has been appointed chief of the Division of Pulmonary, Allergy, and Critical Care Medicine. He plans to expand and strengthen clinical and research programs in asthma, sleep disorders, lung transplantation, and chronic obstructive pulmonary disease, also called emphysema. Choi came to Pitt from Yale University in August. His research focuses on the pathogenesis of adult respiratory distress syndrome (ARDS) at the molecular level.

Choi

Visiting professor of medicine **Thomas Kleyman** came to Pitt in October from the University of Pennsylvania. As the new chief of the renal/electrolyte division, Kleyman plans to add more physician-scientists to the faculty and to expand programs in developmental and cell biology. His research focuses on a kidney protein that is key in regulating blood volume and pressure. *—DH*

CNBC AMONG TOP SIX

The Center for the Neural Basis of Cognition (CNBC) sits solidly among the top six cognitive neuroscience programs in the country. CNBC is a collaboration between Pitt and Carnegie Mellon University; it has been ranked by an advisory board that included members of the National Academy of Sciences and was chaired by Mortimer Mishkin, chief of the section on cognitive neuroscience at the National Institute of Mental Health.

NOT THE USUAL SONG AND DANCE

Which thing is not like the others? A violin concerto, a poetry reading, an Indian dance, a baked Alaska. The med school's Annual Talent Extravaganza in December showcased those who perform in the kitchen as well as on stage. Creations of culinary artists were judged during a dessert contest and, more memorably, consumed at a potluck supper. Students' visual artwork was also on display. (An Irish Dream Cake, made by Audrey Lau, MD '03, and MD/PhD student Kasey Eidson won the dessert contest. Yum.) *—DH*

ARTVILLE

They Fit No Mold

MERIT-BASED SCHOLARSHIP WINNERS

BY ROBERT MENDELSON

GROUP PHOTO ON RIGHT: (Standing from left) Melissa Sherman, Zachary Miller, Sharon Altman, (seated from left) Charley Gates, Cameron McFarland, Sharon Achilles

ARMAND WRIGHT

GETTING INTO THE UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE'S CLASS OF 2004 MUST HAVE FELT GOOD. Getting $15,000 annually for the next four years to help defray the cost of medical school must have felt even better. And certainly, August's White Coat ceremony and orientation for first-year students did nothing to lessen the enthusiasm of the class's six merit-based scholarship recipients.

Then came their first anatomy exam. "It's a good thing you didn't talk to us right after that," they joked almost in unison during a recent roundtable meeting. When it came to the scholarships, they had another nearly unified response: "Why me?" Each more than satisfied the academic requirements, yet it's evident there's no "scholarship winner" prototype:

Sharon Altman, 39, (Medical Alumni Association Scholar) was an award-winning television animator. Her turn toward medicine is an extension of the volunteer work she began after losing many friends to AIDS.

Cameron McFarland, 35, (Medical Alumni Association Scholar) actually dropped out of college at one point. After working as a waiter, he eventually graduated with an English major. Then he joined the Peace Corps and served in Ethiopia, where he taught English and was the liaison between the volunteers and the medical officer. As he dealt with cases on everything from rabies to stomach infections, something felt right. That put him on a path toward becoming an MD.

Sharon Achilles, 30, (Paul M. Rike and Hazel M. Rike Medical Scholar) also served in the Peace Corps; she was stationed in a small West African village. Afterward, she earned a PhD in biology. Her research on new biological methods to prevent sexually transmitted diseases and unwanted pregnancies evolved into a longing to pursue her work on a clinical level.

Melissa Sherman, 29, (Medical Alumni Association Scholar) had been working as an editor of a medical journal. While commuting to her job, she realized she wanted to do more than offer sympathetic glances to the medically underserved population she saw from her perch inside the bus as it made its way through the inner city.

Zachary Miller, 24, (Dean's Scholar) studied biology and sculpture as an undergraduate, then put his creative energies to use in Harvey Lodish's lab at MIT, investigating cancer cell signaling, where neither the aesthetics nor the promise of basic science was lost on him. He hopes to combine his passions for art and science in a way that contributes to bettering patient care.

The youngest of the scholarship winners, Charley Gates, 22, (Paul M. Rike and Hazel M. Rike Medical Scholar) graduated from Notre Dame just last year with a near flawless academic record. (We can see his dad, R. Edward Gates, MD '74, smiling now.) He chose a medical career, in part, as homage to the surgeon who reconstructed his injured knee in high school, which meant he could start on the varsity basketball team the next year. He's hoping to deliver like "miracles" on a daily basis.

These six students fit cleanly into no mold, yet they share at least one common trait: They're wholly committed to doctoring.

FIRST IMPRESSIONS

"I have a hard time seeing patients in pain. . . . I shadowed a palliative care doctor the second week we were here. We walked into the room of a woman whose entire voice box had just been removed because of cancer. She was probably going to pass away, to die. Her family was there, and I could just feel her powerlessness, and her frustration, and her fear."

—Melissa Sherman, MD '04

FIRST IMPRESSIONS

"I don't know if you've ever been to Notre Dame, but just close your eyes and imagine 8,000 of me's walking around—athletic, Catholic, like to study hard, like to play hard. It's a lot more diverse here and that's good. I enjoy that. Definitely."

—Charley Gates, MD '04

Explorations and revelations taking place at the medical school

NATIONAL LIBRARY OF MEDICINE

This illustration, circa 1700, showing an animal-to-human blood transfusion, attests to the desire to replace the essential fluid.

SLICKER BLOOD

A REMARKABLE LUBE JOB | BY DOTTIE HORN

An ambulance, sirens piercing, speeds to help a stabbed man in hemorrhagic shock. He has lost so much blood that his heart isn't getting the oxygen it needs to beat properly. His blood pressure drops. The flow of blood through the smallest vessels, where the nourishment of tissues and exchange of gases take place, falls to near zero. Tissues begin to die.

The ambulance arrives, but ambulances don't carry blood, which the man desperately needs. The emergency technicians infuse saline into his veins in an attempt to restore the volume of his blood to normal. Saline does not stay within arteries and capillaries, but travels through them, requiring that more and more fluid be infused. Even so, saline is the liquid of choice for nonhospital resuscitations. The alternative, a solution containing colloids such as albumin or starch, stays within veins, but can elicit a dangerous allergic reaction.

The ambulance technicians rush into the ER with the hemorrhaging man. Physicians and nurses prepare for a transfusion; it's their turn to take over the struggle to restore the normal flow and pressure of fluid through vessel walls.

Such struggles began almost as soon as the circulatory system was discovered in 1628, believes Marina Kameneva, associate professor of surgery at the School of Medicine. Artworks from the 18th century showing blood transfusions from animals to humans attest to the desire to replace the essential fluid. Today, despite blood banks, physicians face shortages and the impracticality of using stored blood in some emergency situations—so researchers search for a convenient blood substitute. As of now, the Food and Drug Administration has not approved an artificial blood product for use in humans.

Kameneva is not seeking to develop a blood replacement. A PhD in mechanical engineering, she takes a different approach. Since she began studying blood 25 years ago at Moscow State University in her native Russia, she has asked questions about its mechanical properties. Questions such as—What is its viscosity? What are the characteristics of its flow through microscopic vessels? How can we make it flow better?

In an attempt to answer these questions, Kameneva recently induced severe hemorrhagic shock in rats by slowly taking 50 percent of their blood. She then tried to resuscitate the animals. In her control group, she infused the animals with a solution of saline or colloids. Their blood pressure and blood flow through their tissues improved only slightly, and they all died.

In her experimental group, Kameneva infused a new solution—saline mixed with a tiny amount of a substance she has named HemoMax. The results were dramatic. The blood pressure did not reach normal, but the volume of blood being pumped through the heart improved. In fact, blood flow to tissues increased to levels that were higher than before she induced shock. "Not one animal treated with HemoMax died," says Kameneva.

She has a patent pending on HemoMax, which she created by modifying a substance extracted from plants. HemoMax allows blood to flow more easily through vessels, especially through the microscopic capillaries so tiny that red blood cells must alter their shape in order to squeeze through. She is conducting further tests, yet believes the compound could be used to treat not only hemorrhagic shock but also the host of other diseases that affect circulation through tissues, including diabetes.

Kameneva's invention has been dubbed the "STP of blood," which is not so far off. "We make blood slippery," she says. "Blood is flowing faster through small vessels because it's getting this additive."

It makes perfect sense to Kameneva that she would apply her understanding of petroleum engineering to blood. In terms of flow, the hydrodynamics are the same. However, blood is far more complex than petroleum—it is alive, subject to numerous pathological variations, and full of gases, nutrients, and cells. "It's an amazing fluid," Kameneva says. For her, it's more appealing to study than "Texas tea." ■

THE LIFE YOU SAVE MAY BE YOUR OWN

At any given age, a man is more likely to die from a heart attack than a woman of the same age. At age 40, he is six times as likely to die. At age 50, four times as likely and at age 80, he is twice as likely. Marina Kameneva, professor of surgery, asked why.

Kameneva compared the blood of 47 premenopausal women with that of 50 age-matched men. The male blood was more viscous and its red blood cells were less capable of changing shape, less "deformable." Red blood cells, however, need to be supple. They are typically eight microns tall, and must maneuver through capillaries with diameters as small as three microns. The stiffer male cells might never make it.

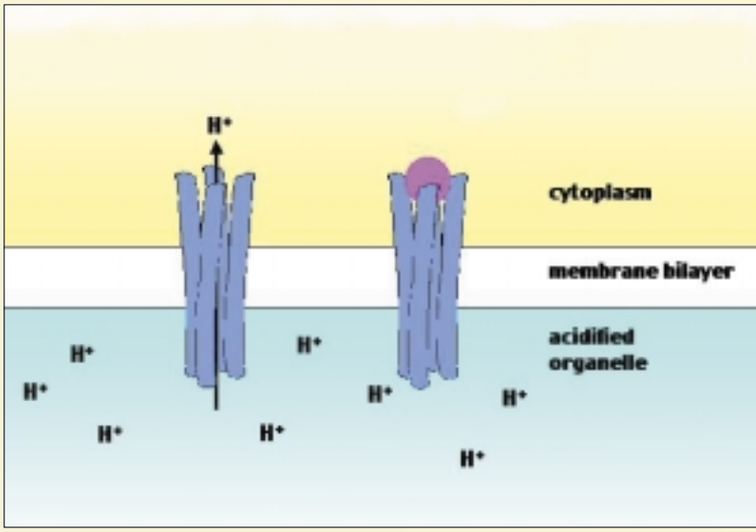
Premenopausal women's blood flows better because it is younger. Menstruating women lose red blood cells every month, and the body replenishes the lost cells with new cells. As a result, premenopausal women's blood has 80 percent more young red blood cells and 85 percent fewer old red blood cells than male blood. The young cells are less dense, which means freer-flowing blood. The young cells also are more flexible, slipping through capillaries more easily.

You don't have to menstruate to rejuvenate your blood; you can simply donate it. One study of middle-aged men found the risk of heart attack 86 percent lower among blood donors. Consider calling the Red Cross today. *—DH*

DRAMATIC ORGANELLES

WEISZ EXPLORES THE GOLGI

BY REBECCA SKLOOT AND ERICA LLOYD



TOP: COURTESY WEISZ ; BOTTOM: KAPELEWSKI/CIDDE

ABOVE: Weisz (middle and seven-months pregnant) with lab crew (from left) Gregory Gibson, Mark Ellis, and Jennifer Bruns. TOP GRAPHIC: Weisz selectively alters the pH of the Golgi apparatus by expressing M2, an influenza protein. M2 channels hydrogen ions from the Golgi's acidic compartment into the neutral cytoplasm, which equalizes the pH. When M2 (shown above in blue) is blocked with certain drugs—e.g., an antiviral compound (purple ball)—it cannot alter pH.

Few people pay attention to the cellular bodies called organelles; even fewer can say there's one they truly love. Ora Weisz is different: She will tell you the Golgi apparatus is her favorite.

Each organelle, like an organ, takes on a specific task—some break down carbohydrates and detoxify drugs, others transport enzymes that keep the cell clean. Among other responsibilities, the Golgi's duty is to receive and ship proteins—it processes the prized freight, then routes it to various locales. Weisz thinks the Golgi looks like a stack of flattened bricks connected end-to-end by a long ribbon. Those "bricks" are really cisternae, a series of continuously changing caverns through which the cell smuggles proteins, later to be released into the cell encased in bubble-like transport vessels created from the Golgi's surface.

Weisz is an assistant professor of medicine and of cell biology and physiology at the School of Medicine. She admits, by the way, that she also is fond of Elvis Presley memorabilia and has taken to collecting it. The stuff is a bit kitschier than organelles, yet she thinks it's still pretty neat. She couldn't tell you exactly what draws her to the King, however. But why she admires the Golgi, the organelle charged with the weighty task of putting a protein—the fiber of life and death and health and disease and growth and aging—where it is supposed to go, well that's clear enough.

How the Golgi accomplishes its tasks is not so clear. "Ten years ago we thought we knew the Golgi," says Weisz. "Yet every few years there's a huge uproar about exactly what's going on in there."

Weisz has spent years studying cellular protein trafficking. These days, she is examining how proteins get around in epithelial cells, which communicate between the body and its external environment. Epithelial cells line body cavities, cover the body as skin, and set up gateways at any surface that interfaces with the world. Because epithelial cells face two distinctly different worlds, they have two distinctly different functions. They line the walls of our intestines, for example, where they absorb nutrients, then transport them to the blood. To accomplish this, the cell surface facing the digestive tract has proteins that import, and the cells on the opposite side export. These cells are polarized—they have different proteins at each pole. If this polarity tips off balance, things can go awry.

For example: "A huge number of cancers affect epithelial cells, and one of the first things that happens is you get a loss of polarity," says Weisz. "So trying to understand what is important in developing and maintaining polarity in normal cells is the obvious first step for understanding it in disease."

Weisz asked the question: *How do these surface proteins know which pole to go to?* One thing the scientific community knows for sure is that the compartment in the Golgi where proteins are sorted for delivery to either pole is the only acidified environment proteins see on their way to the membrane. She tried to alter the Golgi's pH to see what would happen but ran into a problem. The only means for altering organelle pH is through compounds that simultaneously change the pH of all organelles. Weisz couldn't change the Golgi's pH without changing the pH of every organelle.

"You're knocking out all the acidification in a cell and then trying to ask what happens to one small step in the trafficking," she says. Weisz had effectively taken a sledgehammer to the problem.

She was, however, able to come up with a way to use an influenza protein, called M2, to selectively alter pH in certain polarized cells. "The way I was trained," she says, "if you don't have a piece of equipment you need, you make it." Weisz is still refining the M2 method, but has already used it to dispel a popular hypothesis regarding a defect in acidification related to cystic fibrosis.

M2 has refueled Weisz's explorations of that mysterious network of passageways known as the Golgi. "It's just so beautifully organized," she says with a smile. "It's got so many functions and levels of complexity essential for cells, it's quite amazing. More than anything, it's a dramatic organelle. We should know more about it than we do." ■

LATENCY AND TB

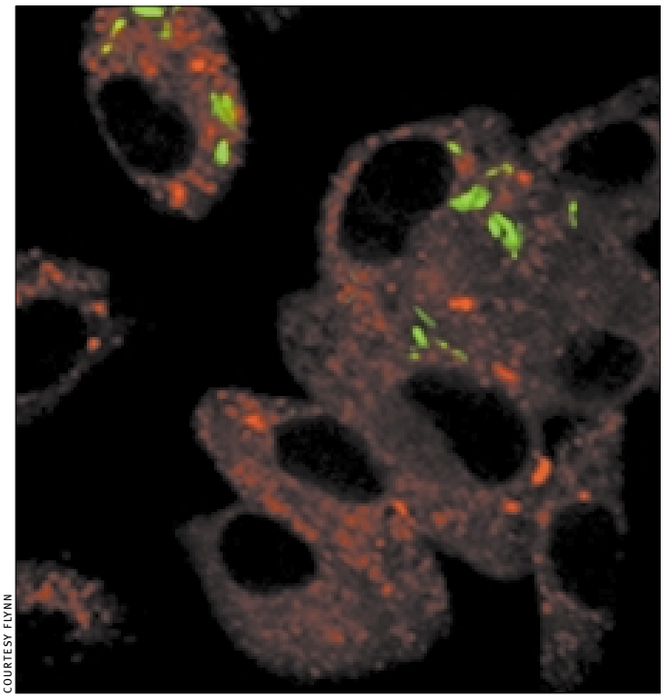
WHAT KEEPS THE DEADLY PATHOGEN AT BAY? | BY ERICA LLOYD

Overheard: Two men on a sidewalk, catching up. One leans in as the other sits on a window ledge and does the talking. He tells the story of how he ended up in not only the same hotel, but the same *room* where the cops raided them that time. Wild. He was living at the shelter, see, then a nurse told him he had to stay alone in the hotel for a few weeks. They thought he had TB. He did. It was kind of crazy, hospital tests—but he's okay now. . . .

One third of the world's population is infected with *Mycobacterium tuberculosis*, the deadly pathogen that causes tuberculosis (TB). TB infections often start out sculpting porous lesions in lungs, and they can make their way to the lymph node, blood, and other organs. The threat of TB is made worse by the recent occurrence of strains that are resistant to traditional treatments. One characteristic of the infection makes those frightening data a little easier to deal with: In 90 percent of the two billion people with *M. tuberculosis*, the mycobacterium will lie latent. The other 10 percent are likely to develop TB in their lifetimes.

How is it the man overheard on the street falls into that unlucky 10 percent? A physician is likely to tell you that his immune system was somehow compromised—perhaps through drug abuse or malnutrition—and that the risk of contracting the pathogen (which is transmitted through the air) is higher among those living in crowded quarters. But if you ask why that particular man ended up with TB and not the guy sleeping next to him at the shelter—who also has a one-in-three chance of harboring the infection—your question is liable to be received with a shrug and a head scratch.

Genetics is known to have a role in some immune functions, yet no one knows why the TB organism remains happily latent in some and sets out on a course of destruction in others, killing three million people every year. (The current vaccine's effectiveness varies widely among adults and is not generally administered in the United States.)



COURTESY FLYNN

Macrophage vacuoles (red) serve as the main hosts for *M. tuberculosis* (green). In about 90 percent of infected patients, the macrophages are able to control the infection so that TB doesn't develop. Flynn wants to know how.

"It comes down to what happens between the host and the organism," says JoAnne Flynn, a PhD and an associate professor in the Department of Molecular Genetics and Biochemistry. To examine the host/organism interaction, she created a latent infection in vivo, no simple task. "We're trying to model something we don't understand," says Flynn. She and other immunologists don't know if the mycobacterium is replicating, morphing, or sitting still during those "latent" periods. They are pretty sure of a few things though, like the role that CD4+ T cells play in keeping TB infection at bay—or at least they used to be pretty sure. CD4+ T cells make a key cytokine (interferon gamma). That cytokine tells the macrophage housing the *M. tuberculosis* to stop being such an accommodating host and to kill the pathogen by releasing nitric oxide. It appeared that if you could use CD4+ T cells to keep the macrophages activated, you could control the bug. Flynn decided to find out what would happen if she took CD4+ T cells out of the equation.

First she created a stable and chronic *M. tuberculosis* infection in mice; then she used antibodies to destroy their CD4+ T cells. Not surprisingly, the mice contracted TB and died. *Yet, somehow, their macrophages were still activated.* It seems CD4+ T cells are necessary to prevent widespread infection but don't work alone.

These days Flynn is scratching her head a bit, but she has reason to be optimistic. She has a workable in-vivo model that's allowing her to decipher elements of the immune response, including the roles of other T cells. And she's convinced the only way to develop an effective vaccine is by first pinpointing exactly what's happening at this level—even if it means lots of head scratching. ■

FOR MORE INFORMATION: Search vol. 192, p. 347 at http://www.jem.org/search.dtl

SUPERCOMPUTING SUPERCHARGES BIO-DISCOVERY

BY DOTTIE HORN

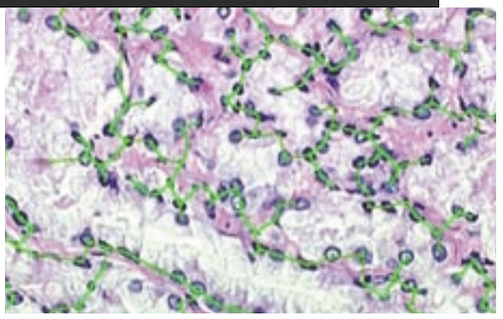
KA-POW!

A pathologist peers into her microscope, studying cells from a prostate tumor, slender stems forming serpentine curves. She examines the amount of tissue between tumor cells, the size of the nuclei, and many other aspects of the cells, which have been stained with special dyes to make their features more visible. She looks at several different slides of the same tumor. She then grades the tumor, assigning it a number from one to five that ranks its severity. She thereby plays a key role in determining how that tumor will be treated.

It's not at all unlikely that the grade she assigns would be assigned differently by another pathologist.

"Grading is one of the most critical parts in the classification of cancer, but it's also one of the most subjective," says Michael Becich, associate professor of pathology at the University of Pittsburgh School of Medicine. He believes survival rates for those with prostate cancer would improve if tumor grading were more objective, so he taught a machine with superhuman capabilities to help pathologists with their jobs.

PHOTOGRAPHY | CRAIG THOMPSON



Using a supercomputer, Michael Becich is building a sophisticated matching system to help pathologists grade prostate tumors. One trick the supercomputer uses in its analysis is a spanning tree (right), formed of lines that connect the cell nuclei. More severe tumors mean longer line segments and sharper angles between segments.

To do this, Becich relies on the system at the Pittsburgh Supercomputing Center (PSC). To the uninitiated, a supercomputer may seem mysterious, an all-powerful, incomprehensible entity. In truth, a supercomputer is not fundamentally different from a personal computer. The processors that make up its basic components are about as powerful as the processor found in today's leading desktop computers. It's the number of processors—500-plus in PSC's current machine—which makes the supercomputer so imposing. The processors are linked, so that some or all of them can work on a project at once.

Actually, a human being could perform all the calculations that a supercomputer does . . . given time. That's the catch: *Nobody* has that much time.

PSC's system is hundreds of times faster than a desktop computer, and it's about to get faster. PSC just got a turbocharge from the National Science Foundation (NSF). After intense lobbying from scientists throughout the country who made the case that an even more powerful supercomputer was needed to advance nonmilitary research, the agency chose PSC as the site for a $45 million terascale Compaq system capable of six-teraflop processing; the system should be completed this fall. In case you haven't been keeping up with your latest issues of *Supercomputing Today,* a teraflop is a trillion calculations per second. In other words, PSC's new system will be able to perform 1,000 calculations for every person on the planet in just one second. With 2,728 processors, each four times faster than today's best desktop processors, the terascale supercomputer will have a peak speed 13 times faster than PSC's current machine. It will be 10,000 times more powerful than a desktop computer. PSC's existing system is fast, no doubt. Its new terascale system will be what scientists refer to as *really fast*. It will give them the capability to do what, until now, they have only imagined.

"You attack a totally different set of problems if you have that speed at your fingertips," says Ralph Roskies, Pitt professor of physics and coscientific director of PSC, which is a collaboration between Pitt, Carnegie Mellon University, and Westinghouse Electric Company.

Roskies likes to compare supercomputers to cars. A car does little beyond moving you faster than you would otherwise, yet cars have totally transformed society. Likewise, a supercomputer's primary asset is speed. And likewise, the supercomputer's speed is transformative—allowing scientists and engineers to shed new light on old problems. Using PSC, astrophysicists are simulating black holes, meteorologists are developing more precise weather forecasts, and engineers are designing more efficient power-generating turbines. In the biomedical arena, all that computational power has gone straight to some researchers' heads, in the very best sense. It has given some creative minds a powerful tool in their examination of wellness and disease, and in their approaches to diagnosis and treatment.

Becich's supercomputing access meant he could be more inventive as he thought about how to improve the lot of the some 180,000 American men diagnosed each year with prostate cancer (nearly 32,000 of whom die).

What he came up with is a quality-assurance tool to aid pathologists in grading prostate tumors.

To create this tool, Becich gave the supercomputer the oncological equivalent of a handwriting-analysis lesson. This is how his system works: Becich gives the supercomputer a slide that has been converted into a numerical format a computer can recognize. The computer studies the tumor and calculates its "digital signature." The signature is like a list of vital statistics. It describes those features of the tumor that have proven most useful in enabling the computer to distinguish among the five grades. For example, the signature includes stats based on the tumor's "spanning tree"—a branching, angled line that connects all of the cell nuclei in the shortest possible route. In the higher grades of cancer, the spanning trees have longer line segments and sharper angles between line segments, which means a tumor is more severe. Likewise, shorter line segments and softer angles signal less-advanced tumors.

The supercomputer then compares that digital signature to what is in its storehouse—a computerized gallery of prostate tumor images. The computer has already calculated the signature for each image in its storehouse, which also has been graded by an expert pathologist. The computer hunts through the storehouse to find images that most closely resemble the unknown tumor and gives the pathologist a ranked list of likely matches. The pathologist can then view the matching tumors and the grades assigned to them.

Pathologists won't need supercomputers to use Becich's diagnostic tool. Becich is applying what he is learning from his PSC work to build a diagnostic aid that pathologists can run on a desktop computer using a CD-ROM.

Becich's work could help pathologists throughout the world with their diagnoses. He has grander plans, too. A while back, he started to wonder if the supercomputer could actually teach humans new ways of looking at tumor cells.

Becich has found a way to get the supercomputer thinking for us: In research he's planning, the supercomputer will analyze data from 600 prostate cancer patients. The data include slides of the patients' tumors, along with details about what happened to each patient over a 10-year period. The computer will then group together those patients whose disease followed the same course, regardless of the grade assigned to their tumor. For example, it will group those who developed metastatic disease. The computer will look at all the slides from these patients and ask, *What features do these tumors share that are not present in the tumors that proved to be less aggressive? How might we predict from the slides which tumors will progress to metastatic disease?*

"The fun part is letting the computer go free and saying, find me all the features that predict these bad ones," says Becich.

The work of assistant professor of anesthesiology Pei Tang is, in supercomputing jargon, *computationally intense.* In other words, it requires a lot of effort on the part of the supercomputer—zillions and zillions of calculations. When Tang submits a project to PSC, the center usually dedicates 128 processors to it, and each processor works for 240 hours—10 days—to finish the job.

Tang's goal is to understand how general anesthesia works its magic, rendering people unconscious, ensuring they feel no pain during surgery, and leaving them with no memory of the operation. Though general anesthesia has been used for more than a century, no one understands why or how it works. In her attempt to lay bare the mystery, Tang decided superhuman, or at least supercomputational, methods were in order.

"You attack a totally different set of problems if you have that speed at your fingertips."

Like any investigator who wants access to PSC's behemoth system, Tang submitted a proposal for supercomputing time—competing with scientists from across the country. Because of the computational intensity of Tang's project, a panel appointed by NSF reviewed her proposal. (Smaller runs can be approved internally at PSC.) As a noncommercial researcher, Tang was awarded time on the machine for free.

Tang, who is a PhD and chemical physicist, is determined to unveil what's happening at the molecular level when someone is anesthetized. Although laboratory techniques such as crystallography can provide still representations of molecules, computational modeling allows Tang to see how molecules move individually and at split-second intervals. Before the computer can determine how the molecules will move, Tang must first describe all the atoms involved. No simple task. She starts with a general physiological situation she wants to model and then creates a lineup and stats for every single atomic player.

From her laboratory experiments, Tang knew that anesthetics affect cell membranes, particularly the ion channels through which ion particles pass in and out of the cell. Cell membranes are complex, so Tang created a simplified model of a membrane and an ion channel traversing it.

Tang describes her model as a sandwich. Imagine a double hamburger—bun, meat patty, meat patty, bun. The two inner layers—the meat patties—are the lipid bilayers. Semipermeable, water-repellent, and made of fats, these lipid bilayers are basic ingredients in cell membranes. The two outer layers—the buns—are the water molecules that surround cells in abundance. Imagine a straw going all the way through the sandwich from top to bottom. This is the ion channel. In her model, molecules of halothane—the anesthetic Tang chose for her model—interact with this simplified representation of a membrane.

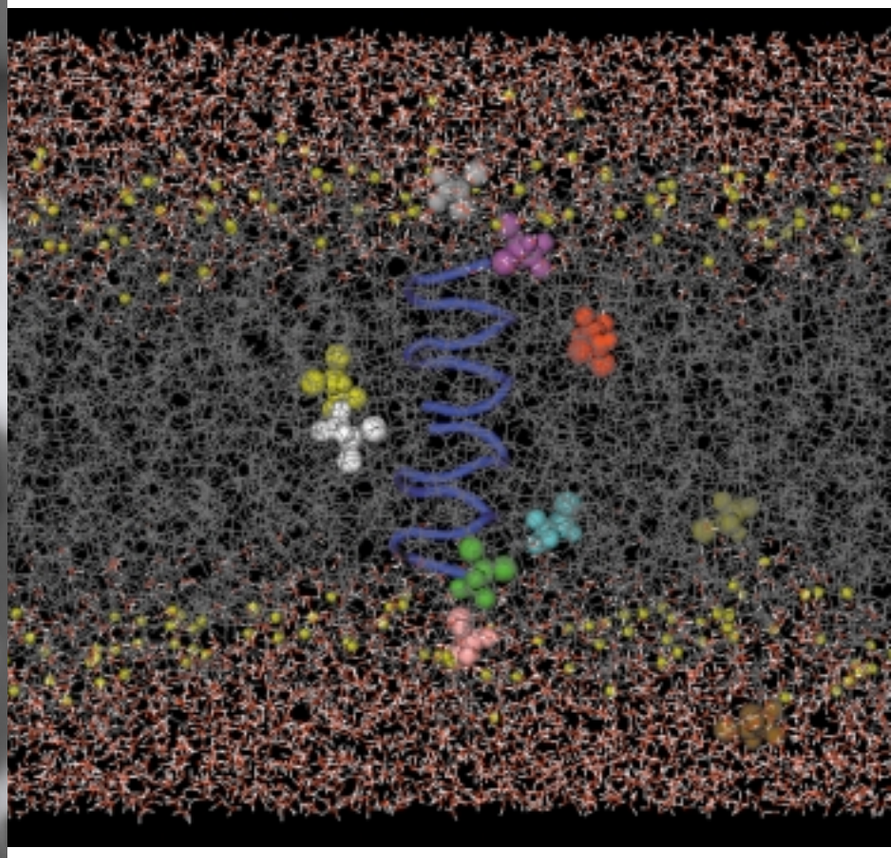
Her next step was to specify exactly how many molecules would be part of the model—5,538 water molecules, 182 lipid molecules, 10 molecules of the anesthetic halothane, and one macromolecule of the protein gramicidin, which single-handedly forms the ion channel. She next broke each molecule down into its constituent atoms—16,614 atoms from water, 21,476 from the lipids, 80 from halothane, and 552 from gramicidin. One measuring stick for a simulation is the number of atoms it contains. At 38,724 atoms, Tang's system is considered huge.

Tang's next job was to describe the features of every single atom, including its relationship to each of the other 38,723 atoms, in the only terms the computer understands—numbers. Her numerical portrait of each atom delineated characteristics such as the attractions and repulsions among atoms. She compiled a host of descriptive details for every single atom.

Then it was time to let the supercomputer stew. She gave it the information about all the atoms. She gave it the laws of physics that allow her to calculate the atoms' activity.

The supercomputer's job was to track the atoms for two nanoseconds (a nanosecond is 10^{-9} or .000000001 second). That couldn't take much time, right? Wrong. Remember,

Tang's goal is to understand how general anesthesia works its magic, rendering people unconscious, ensuring they feel no pain during surgery, and leaving them with no memory of the operation.



Pei Tang is shedding light on the mystery of anesthesia. In her simulation (above right), the clustered balls are anesthetic molecules, which appear to gravitate to the entry to the ion channel (blue spiral) and the interface between the water molecules (dark pink) and the lipid bilayers (yellow).

Tang's work is computationally intense—one run takes 10 days. Here's how the supercomputer spends those days:

To get a slow-motion picture of those two nanoseconds, the computer breaks time into femtoseconds (femto is 10^{-15} or .000000000000001 second), and takes a numerical snapshot at each femto-interval. It captures the atoms at a given instant by calculating all the physics equations for the set of nearly 40,000 atoms—which takes a single processor about a minute. Then it moves forward another femtosecond and churns through the equations again. And again. And again. There are a million femtoseconds in a nanosecond, so the computer must run through the calculations *two million times*. Simulating what happens to the atoms during two nanoseconds ends up taking 30,720 processor hours. (A processor hour is an hour on one of the supercomputer's many processors.)

What the supercomputer finally spits out at the end is a bunch of numbers—an account of the atoms at each femtosecond slice of time. Software converts the numbers into an animated movie, stretching the two nanoseconds into several seconds so that human eyes can watch the molecules in action.

Tang's simulation shows that the halothane molecules tend to go to the region where the lipid and water molecules meet. They are drawn to a particular segment of the gramicidin found on each side of the entry to the ion channel.

Her persistence is paying off: A revealing picture of halothane is emerging.

Tang, however, expects to create many more models in her efforts to crack this mystery of consciousness that has lasted 100 years.

James Antaki got tired of taking stabs in the dark—that's why he has turned to PSC.

Throughout the past 50 years, researchers like Antaki have tried to find a safe way to pump blood artificially in patients whose hearts are failing. Initially, they removed the

diseased heart and replaced it with an artificial one, but that increased blood clotting. Later, they found that, instead of removing the heart, they could implant a booster pump to supplement or take over its function. The booster pumps, however, also have blood-clotting problems and are not considered safe for long-term use. They are used only as a stopgap measure to hold off death in the hope that a donor organ can be found for a heart transplant. If, however, these pumps were safe enough to be implanted for years rather than just months, they might serve as an alternative to heart transplants. Today, some cardio researchers see the design of a safer pump as the brass ring.

Their efforts are hit-or-miss. They speculate that a particular alteration will have a desired effect and then build a model to test their theory. There's a smarter way to approach redesign, believes Antaki, who is an associate professor of surgery and mechanical engineering at Pitt. He contrasts the design of heart pumps to that of aircraft. Today, the airline industry would never develop an aircraft propeller design through guesswork. It would never evaluate the design by building the propeller, installing it on a plane, and taking the plane for a test flight.

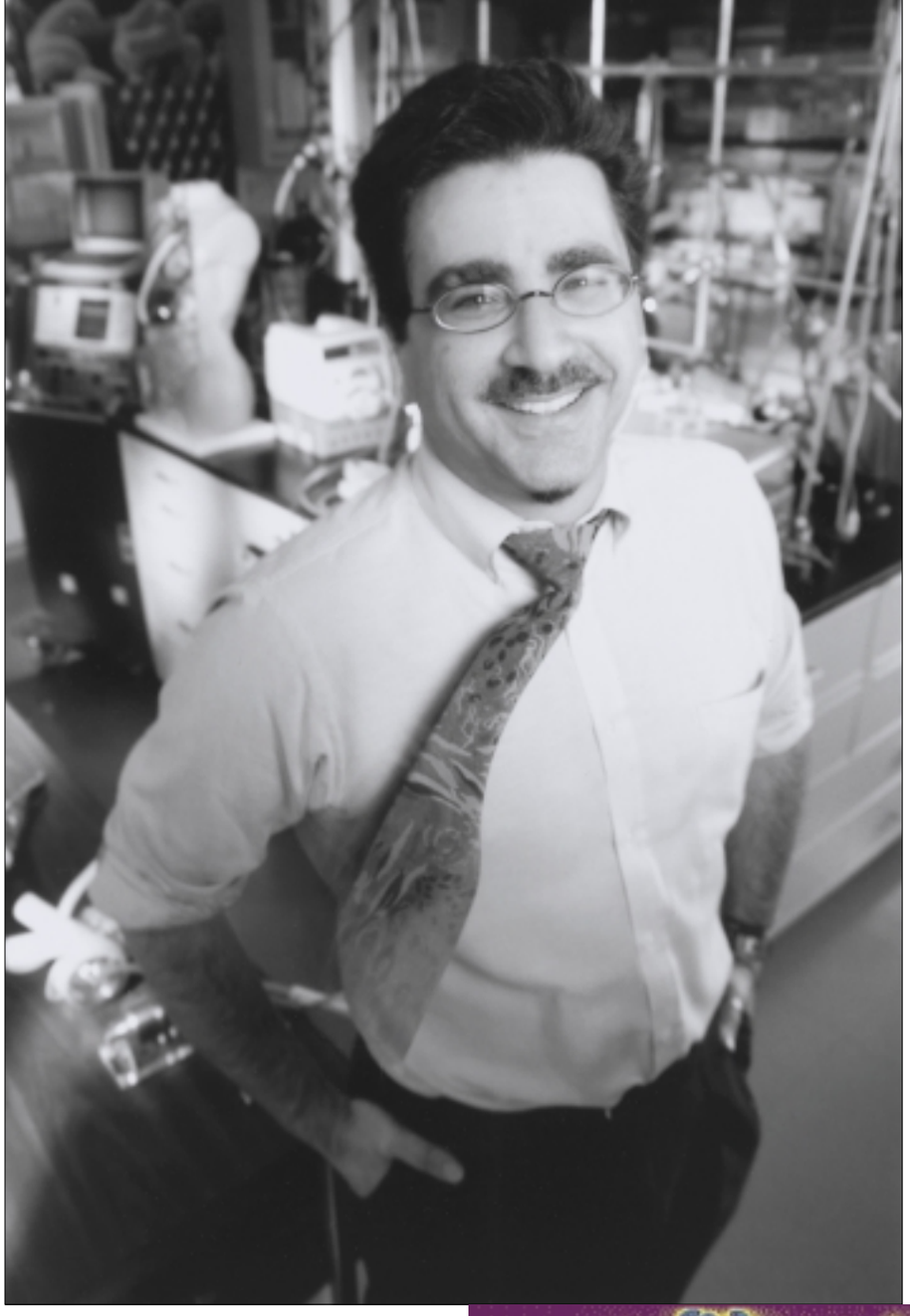
"The aircraft industry has sophisticated mathematical and numerical models that facilitate the design of safe, economical aircraft, while the analogous models for artificial organs are still in an embryonic stage," wrote Antaki in a recent proposal to NSF. He wants to bring pump design into the jet age.

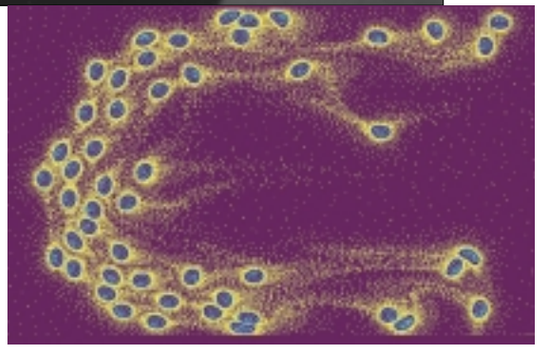
The proposal submitted by Antaki and his collaborators, including Omar Ghattas of Carnegie Mellon University, who is the principal investigator, was one of only 63 funded out of 1,400 submitted to an NSF program supporting information technology research. They were awarded $4.9 million to create blood flow models that will expedite the design of a better heart pump. By the time they've finished the project, they hope to have modeled tens of thousands of red blood cells suspended in fluid. They'll use the supercomputer to track the activity of the cells—how they clump, alter their shape, rupture, bounce off one another, flow in a variety of conditions, and become damaged by the pump.

The task will not be easy. Currently, no techniques exist to model the flow of bodies that interact and collide. NSF has given Antaki and his collaborators five years to develop computational methods to harness the supercomputer's power. If they succeed, they will have built the most detailed, realistic model of blood flow ever made.

Then they can make a calculated and well-rehearsed lunge for that brass ring—a truly safe and effective heart pump.

Given the track record of the hardware industry, it may be that one day we'll all have terascale computers on our desks. That's when Ralph Roskies and his colleagues at PSC will be off building a computer some-multiple-of-a-trillion-scale, a system so powerful we'll have to make up new prefixes, expand our language. And all those processors chugging away, churning out a godzillion calculations every Zen-second—they'll just be working harder and harder to keep up with the human imagination. ■





James Antaki (above) wants to build a better heart pump; to do that, he's constructing blood flow models. Already, his team has modeled the flow of 50 red blood cells (right). Their plan is to model tens of thousands of the cells—to determine where and how they clump, change shape, become damaged by the pump, and flow under various conditions.

ALUM STEVEN C. BEERING PUT PURDUE WAY UP THERE

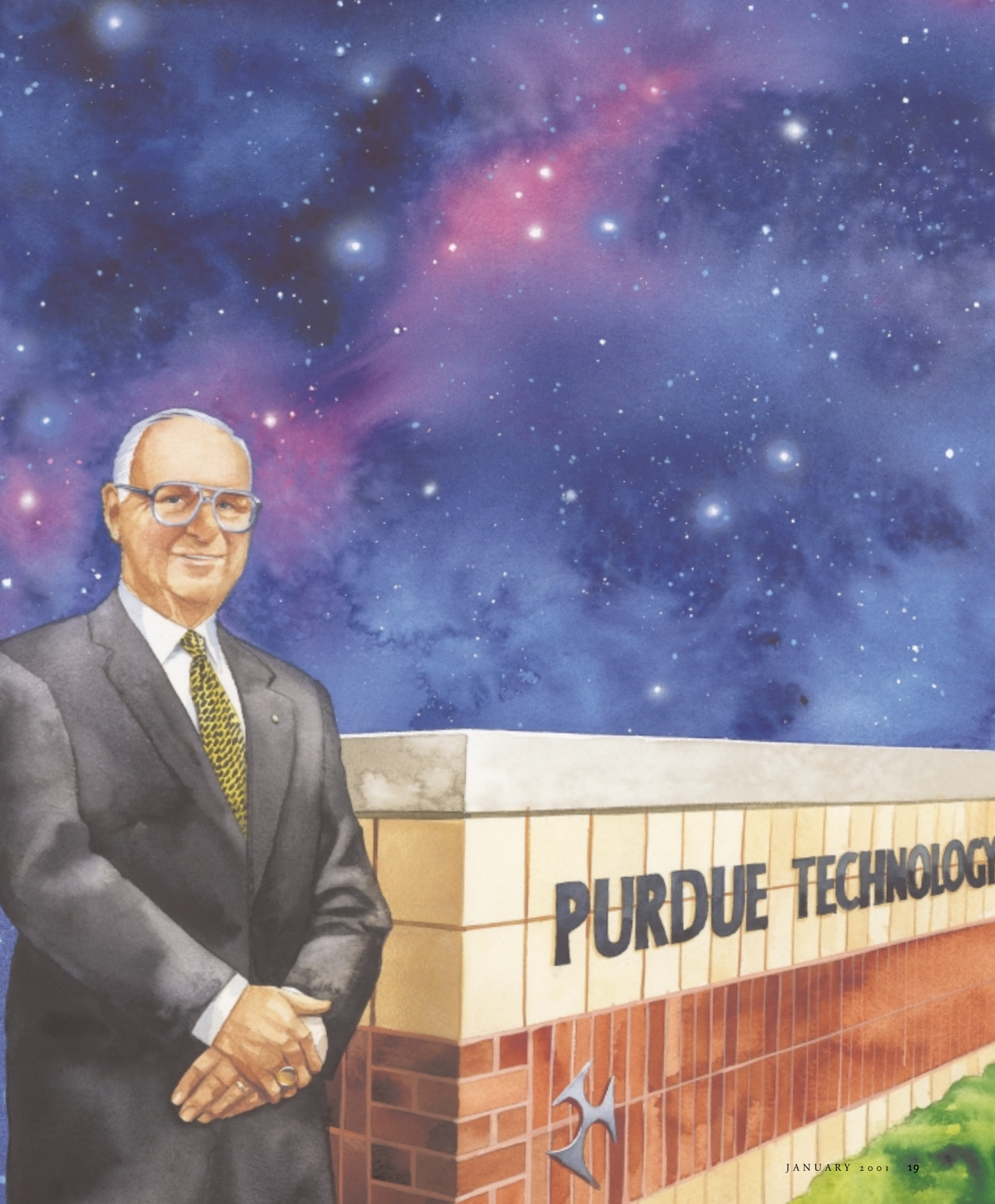
BY WALTON R. COLLINS

HIS PERSONAL COSMOS: INDIANA

On an October evening in 1999, 18 American astronauts sat down to dinner in West Lafayette, Indiana. At the table were Neil Armstrong, the first human being to walk on the moon, and Eugene Cernan, who was the last. Another diner was David Wolf, who lived aboard the Russian space station Mir for four months and boasts more time in space than any other American except Shannon Lucid.

The host of this exceptional gathering, Steven C. Beering, MD '58, recalls the night as one that never quit. "They didn't want to leave," he says. "They just huddled together. David Wolf wanted to know what it was like to land on the moon, and Neil Armstrong was immensely curious about what it was like to fly with the Russians. David—of course—holds the pioneers on a huge pedestal, as we all do, but at the end of the evening he realized that what he had done was exciting and important too, and valued by the older astronauts. It was the next step, and they regarded him as a pioneer, as he did them.

ILLUSTRATION | MIKE MCQUAIDE


PURDUE TECHNOLOGY

"I couldn't sleep all that night, I was so excited," Beering recalled recently.

It takes something pretty unusual to give Beering a sleepless night. After graduating from the University of Pittsburgh with a BS in 1954 and an MD in 1958, Beering went on to become a physician to astronauts, architect of a medical education system copied across this country and overseas, and dean of one of America's premier medical schools (Indiana University School of Medicine). He has accumulated eight honorary doctorates and conferred 350 others on a heady list of national and international dignitaries.

Honors from his alma mater include the Distinguished Alumni Fellows Award, an honorary Doctor of Science, the Philip Hench Distinguished Medical Alumnus Award, and the University's Bicentennial Medallion of Distinction; the last award has gone to only four other persons, two of them posthumously. And he was recently appointed to Pitt's Board of Trustees. His community honors include the titles Sagamore of the Wabash, the state of Indiana's highest honor, and Kentucky Colonel, which his neighbors in the state next door bestowed on him. That barely gets through the first page of his weighty curriculum vitae, though there's one other line on Beering's CV that especially stands out: President, Purdue University, 1983 to 2000.

After presiding for 17 years over one of this nation's top public research universities (a ranking Purdue could not claim before his tenure), Beering stepped down in August. He has moved out of the presidential residence and turned his office over to his successor, Martin Jischke. Beering and his wife, Jane, whom he met when both were Pitt undergraduates, will continue living and working in West Lafayette. Beering, who graduated more than half of Purdue's living alumni, will continue serving the university as a key envoy.

Jischke, who comes to Purdue after having served as chancellor and president to other universities, may want to start dining with astronauts, too. After all, these are folks whose most memorable views of Indiana are from hundreds of thousands of miles away—and it seems that one charged with running a university needs to elicit a healthy lot of "big picture" perspectives, no matter how much experience one may have. Imagine the university president's job description: Figure out what the next couple of generations need to know to succeed, lay the groundwork for a new era of discovery, shepherd our society's intellectual future. Under "Additional Responsibilities" it would say something about partnering with the community and making no enemies. No wonder university presidential terms have shrunk to less than seven years in the last decade. Beering's 17-year tenure puts him in an elite group.

When Beering arrived at Purdue in 1983 as the school's third president since the end of World War II, not everybody on the faculty was thrilled at the idea of a medical doctor leading their institution; some grumped that he didn't have a traditional academic background. At such a moment, faculty members are looking for clones of themselves, notes Robert L. Ringel, who worked closely with Beering for those 17 years as dean of the school of liberal arts, dean of the graduate school, and executive vice president for academic affairs. "They want someone who will put their needs right at the top," says Ringel. Yet: "People came to accept the president's ability to set priorities."

A college faculty is far from the only constituency that tests presidential mettle. Members of the board of trustees demand tangible results. An unguarded presidential word at a state budget committee hearing can jeopardize funding for an entire biennium. Alumni and benefactors have to be cultivated so that they support their alma mater through thick and thin, even bad football seasons. Then there are the students, some of whom are convinced they could run the university a lot better than that most pejorative of words in the student lexicon—the "administration." And who knows when a "gotcha" journalist might pop out of the bushes? This is a job where the consequences of error run high.

If you asked Robert L. Ringel to describe the ideal university president, he would likely answer with a series of abstractions: decision maker, delegator, fund-raiser, supportive administrator, with a good memory for names, faces, and personal details and credibility in dealings with state legislators. For Ringel, Steven Beering fleshes out all those abstractions: "He has made tough decisions, but he has managed to touch the heart of the university in terms of what it can do, what it should do, and what it can do well.

"Steve is Steve," says Ringel, "whether it's Monday morning in the office or Saturday afternoon on the golf course or Tuesday morning counseling a friend who has called to say his spouse, or her spouse, is ill. This consistency . . . leads to a much-valued genuineness."

University presidents are never off stage. "In the union building at lunch," says Ringel, "Steve will sit down with a group of students—take his tray over and sit down and say, 'Hi, I'm Steve Beering.' I've seen him do this in buffet-style restaurants in the community, too. He knows a university president is a leader and a public person and has to be approachable."

Nor are their schedules flexible. David Beering recalls what it was like to be the son of a university president: "We'd plan major events . . . around the university's official schedule. We knew we were not gonna get married in June." In fact, sometimes Beering-family quality moments ended up including tens of thousands of other people. David Beering remembers sitting among his classmates during his 1985 commencement as his father stood at a podium reading an anonymous letter written by a parent to a graduate: "The relationship between parents and children has to survive a lot of stress through the years," he read from the letter. "This is because each of us starts out expecting too much of the other. . . . We have grown up when we accept each other as we are. I think you are now old and wise enough to love an imperfect father. . . ."

Not everybody on the faculty was thrilled at the idea of a medical doctor leading their institution.

The hall stirred in recognition as Beering directed the letter's closing to his own son, making it clear that, yes, Beering was the anonymous father: "You will encounter obstacles . . . but you will triumph over your troubles, David, just as you managed to cope with the problem of being the son of a university president."

You wouldn't guess it from his nearly unaccented Midwestern speech, but Steven Beering was born in Berlin, in 1932. He arrived in this country 16 years later, after a period in London, and made his way to Pittsburgh in time to graduate with the Taylor Allderdice High School Class of 1950 and go on to Pitt for his BS and MD.

What happened next was the first time Beering's fortunes intersected those of the country's space pioneers. During 11 years in the Air Force Medical Corps—much of the time at Lackland Air Force Base near San Antonio,

The average tenure for a university president has shrunk to less than seven years. Beering served Purdue for 17.

BELOW: (Left to right) Astronaut Gene Cernan, Steven Beering, Neil Armstrong, and Purdue capital campaign cochair Richard Hanson in 1994 at the victory celebration for a Purdue fund-raising campaign.

PHOTO: DAVID UMBERGER/PURDUE UNIVERSITY

Texas, where he ended up as chief of internal medicine at Wilford Hall Medical Center—Beering served on the medical support teams for the Mercury, Gemini, and Apollo programs. An endocrinologist, Beering studied hormonal changes in the body resulting from environmental stress—in an attempt to decipher what would happen to human bodies in space. Some of his research is still classified, so he's not allowed to talk about it in detail.

Beering met Neil Armstrong when the astronaut candidate came through San Antonio for a medical evaluation. Years later on July 20, 1969, when Armstrong descended from the lunar lander to put footprints on the moon, the Beerings were watching from a new home in Indianapolis, surrounded by boxes not yet unpacked after a move from Texas.

A couple of years earlier, Beering had served as a consultant to the state of Indiana, where a debate was raging about whether and where to build a second medical school to help keep physicians in the state. He was part of a governor's commission that designed something radically new in the delivery of medical education: Instead of constructing an expensive new school, it proposed creating cost-effective satellites of the Indiana University (IU) School of Medicine for half of its first- and second-year students, placing them on the campuses of several public and private universities where they could benefit from the science faculties of those schools while getting to know the community. The idea worked, and the plan has been copied extensively, but it was bold at the time. The next thing Beering knew, he was invited to run the program. By 1974, he was serving as dean of IU's School of Medicine. (Mention his name today to many of Indiana's practicing physicians and the word "mentor" will enter the conversation.)

By any measuring stick, Purdue has thrived under its MD president. Ask about the state of the campus when he arrived though, and Beering will wince. Purdue faced problems that plagued many urban campuses; he paints a picture: "There were four public streets going through the heart of campus, the noise was deafening, the smog and pollution tremendous. We had accidents regularly. People on bicycles were hit. So we closed this off and made the space into a mall." Everything about the university grew: new buildings on the flagship campus, four new regional campuses to carry the Purdue name, academic programs, research. Enrollment shot up 27 percent to its current total of 66,500 system-wide.

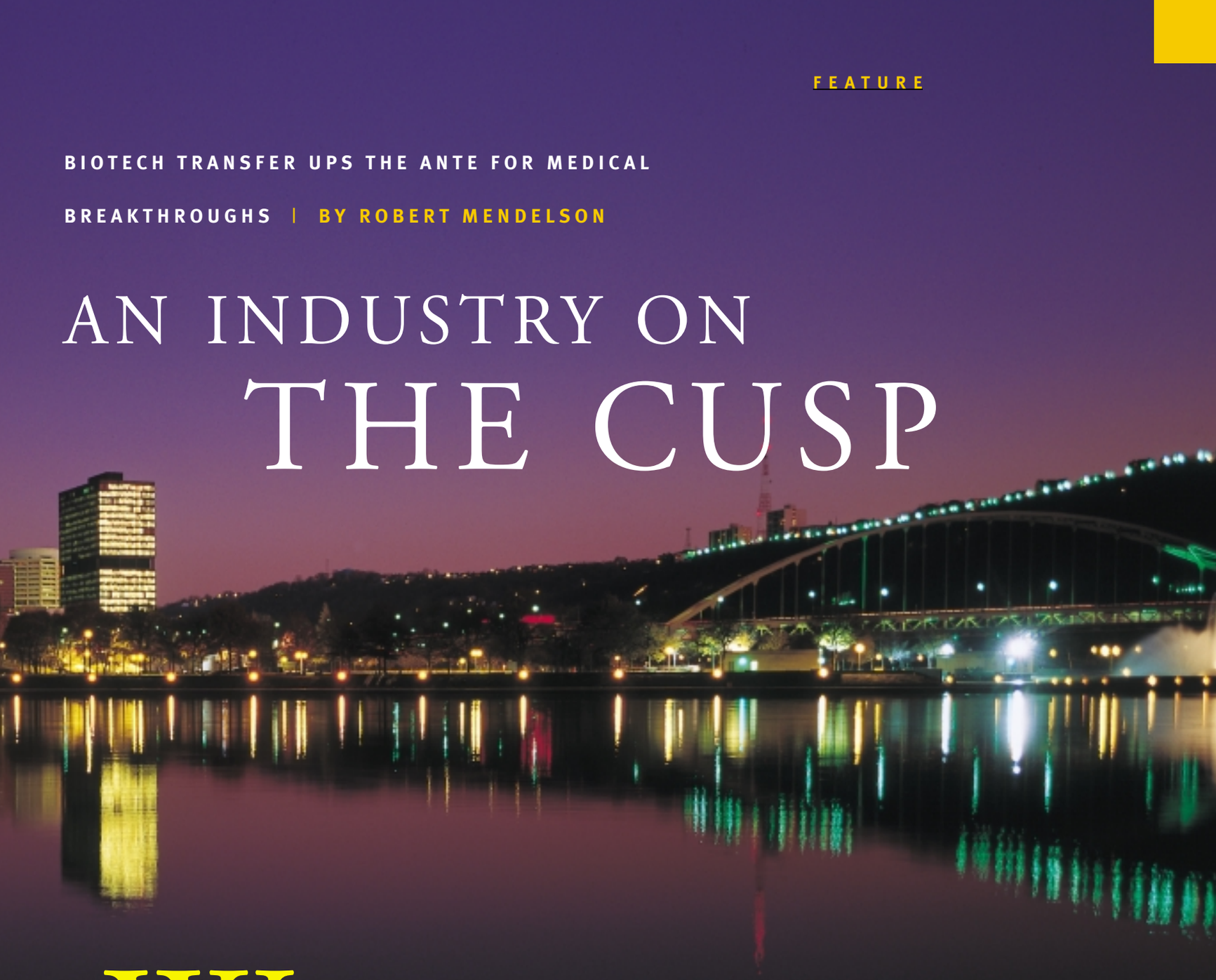
Beering doesn't dwell on bricks and mortar or dollars and cents when he reflects on his time as president. The Pitt alum would rather talk about how he built the largest contingent of international programs of any US university or his strategies for luring exceptional students. And there's the way research has grown. When he arrived, Purdue was doing about $35 million in research; this year it reached $263 million, putting the school among the top public research universities. "I'm immensely pleased by that," says Beering. "That's the lifeblood of the academy—to uncover and discover and to be creative."

Beering's arrival at Purdue reestablished his long association with America's astronaut corps. Through its engineering department (which includes an astronautical program), Purdue has graduated 21 men and women who have flown in space. Beering was at Canaveral on several launch days, but he has never, to his disappointment, seen a rocket lift off. The closest he got was a launch that was scrubbed with three seconds to go. His schedule never allowed him to wait around for the next launch window, a fact he reports with regret but without giving the impression that it shattered a dream.

Despite all the talk of antigravity conditions, one gets the sense that Steven Beering's feet are planted firmly on the ground. Yet he'll enjoy musing a bit on, say, delta-wing spaceships—how someday they'll take off like any airliner, go into space, then return for a controlled landing. "The way we launch now is really a controlled explosion," Beering says, cringing. If that delta-wing ship were rolled out tomorrow, would he volunteer to climb aboard? He laughs and quotes his friend Neil Armstrong's quip about emulating John Glenn's return to space at age 77: "Perhaps when I'm a little older." ■

BIOTECH TRANSFER UPS THE ANTE FOR MEDICAL BREAKTHROUGHS | BY ROBERT MENDELSON

AN INDUSTRY ON THE CUSP



Weaving in and out of traffic. Speeding. Disregarding stoplights. It's the kind of wild ride most 11-year-old boys would relish. Yet the boy in the back seat of his family's minivan isn't shouting words of encouragement to his dad, seated behind the steering wheel. In fact, the sixth grader's eyes are not even open. His mother clutches him tightly. And prays. This is no joyride. It's a trip to Children's Hospital of Pittsburgh.

Only two days ago, he was just like any other energetic preteen. Then, he started to complain that his arms and legs were a little stiff. He was sleepy, too. His parents thought he simply needed a good night's rest. By morning he had developed a modest fever, and he was still tired, so his mom let him stay home from school. At dinnertime, neither his mom nor dad could entice him to come to the dining room table, not even for chicken nuggets.

PITTSBURGH PHOTOGRAPHY | JACK WOLF
PORTRAIT PHOTOGRAPHY | RICHARD KELLY

Joseph Carcillo (left) and Ed Jackson made the walk to the OTM to patent a treatment to prevent acute renal failure, which could save tens of thousands of lives annually. Getting the treatment into clinics isn't so easy, however.

While he lay in bed, his parents placed a call to their primary care physician's answering service. When they checked on him moments later, his fever had suddenly escalated, and he wasn't responding to their nudges. They didn't wait for the doctor's return call.

Intensive care pediatrician Joseph Carcillo had seen this before, about 50 times a year, he estimates. The boy was in septic shock. His immune system was unable to ward off infection. To keep germs from spreading throughout his body, his blood vessels were constricting and his heart wasn't pumping enough blood. The reduced blood flow to the kidneys had caused them to start failing. This condition could be fatal—not an unusual outcome in children or adults. According to the National Institutes of Health, at least 115,000 Americans incur acute renal failure annually, and most experts conservatively estimate 50 percent of those patients will die.

To combat the grave symptoms of his young patient, Carcillo gives him ongoing fluids, starts him on medication to maintain heart function, administers antibiotics to ward off the infection, and puts him on continuous dialysis with the hope it will take over the blood-filtering responsibilities of the kidneys.

Carcillo does nothing, however, to protect the kidneys from the bacterial onslaught. He can't. There is no approved therapy. Even if the boy survives, his kidneys may be damaged to the point where he will need regular dialysis or a kidney transplant.

All Carcillo and the boy's parents can do is wait and hope for the best.

Someday that may no longer be the case. Carcillo, an assistant professor of anesthesiology, critical care medicine, and pediatrics, and his colleague Ed Jackson, a professor of pharmacology and medicine, have an idea that it might be possible to prevent kidneys from shutting down during septic shock. Actually, after years of testing in Jackson's federally funded Scaife Hall laboratory, it's more than an idea. It's a patented treatment that has a few more significant hurdles to clear before it can be administered to patients in intensive care units throughout the world.

If Carcillo and Jackson are correct, everyone wins. Lives will be saved worldwide. Health care costs are likely to go down. And Pitt and its two inventors will probably make a lot of money.

These kinds of breakthroughs haven't always translated into financial windfalls for academia. However, a 1980 bill sponsored by then US Senators Birch Bayh and Bob Dole changed everything.

"That legislation," explains James V. Maher, provost of the University, "assigned the ownership of intellectual property that resulted from federal grants to the universities." Before the act, it was unclear who owned those rights, so it was hard to commercialize anything with confidence.

The business section of any newspaper attests to the act's impact. "It's been a very productive piece of legislation in terms of stimulating the growth of high-tech companies," says Maher. "It deserves credit for an awful lot of the growth that is so evident in the Nasdaq over the past two decades."

To help make its mark on the Nasdaq, in 1996 Pitt instituted an Office of Technology Management (OTM). For the fiscal year 2000, the OTM reported nearly $4 million in revenues and entered into 24 licenses and options. Much bigger checks are expected in the years to come, however.

Nearly 70 percent of the OTM's portfolio stems from the School of Medicine; for the most part, that's pharmaceutical or biological based products. It can take eight to 10 years for these kinds of products to go from a preclinical state to a revenue-generating product, according to OTM officials. The wait has kept Pitt out of the headlines locally.

"One of the things that we deal with in the community," says Reed McManigle, an OTM technology licensing manager, "is they look up the street [at Carnegie Mellon University, which in 1998 generated more than $30 million, primarily from selling the stock of its Internet company Lycos, Inc.]. They deal mostly with software, the Internet, and robotics, which have a much shorter gestation period. They can have a big hit and bring in $20 million in a matter of two years from when it left the university. We're probably doing as many or more deals than CMU, but in terms of visibility in the community, it just isn't there yet because we have a longer gestation period."

Jackson and Carcillo aren't so concerned about timelines. They want to save lives.

Their theory for preventing acute renal failure originated in 1994, after they reviewed the work of others who found that theophylline, a drug used for asthma, reduced the severity and incidence of acute renal failure induced by sepsis. Since theophylline contained blockers of the chemical adenosine, Carcillo and Jackson postulated it was the presence of adenosine in the kidney that facilitated renal failure.

One year later, the poor outcomes of Jackson's laboratory rats made them rethink their position.

WAITING GAME

Imagine: a vaccine for cancer. Olivera Finn, a professor in Pitt's Department of Molecular Genetics and Biochemistry, believes she has such a vaccine sitting in vials in her lab. Her animal research demonstrates that it may prevent more than 80 percent of all carcinomas—including cancer of the breast, colon, and pancreas—by alerting T cells the moment a tumor cell appears. Without it, T cells might not recognize a tumor until it becomes too powerful for the immune system to destroy. Finn is eager to test her patented vaccine in clinical trials designed for persons at a high risk for developing cancer. First, she must convince the National Cancer Institute and the Food and Drug Administration that her vaccine is safe and won't set off an autoimmune response that would harm the people it is supposed to protect. That has been a challenge. Nevertheless, Finn—who is an academic founder of Corixa, the company that holds the license to her vaccine—has faith that it's just a matter of time before her vaccine will be given a chance. Still, she can't hide her frustration: "One in eight women will develop breast cancer. That puts all women, including my 21-year-old daughter, into a high-risk group. Now is the time to vaccinate her, when she is young and healthy, not when she's over 60 and sick from cancer." *—RM*

ON TRIAL

There's a rule: Before a test-tube discovery can turn into a medical breakthrough and multimillion-dollar product, it has to work. First, in animals. Then, in people. Merrill Egorin, professor of pharmacology and medicine, helps make that happen. Egorin lets others do the discovering—he keeps busy testing potential cancer treatments for everyone from university researchers to Bristol-Myers Squibb to the National Cancer Institute (NCI). Pitt is one of only six preclinical trial (animal) funded sites for the NCI, which entails evaluating drugs the agency developed. Egorin also will perform analyses for more than a dozen human trials this year. He'll work with the team of Donald L. Trump, chief of hematology-oncology, which administers the drugs to the patients.

These trials occur in phases: For cancer drugs, phase one establishes safe and effective doses. If all goes well, the drug is used to treat patients in phase two. Should they respond favorably, the drug enters a phase-three trial, comparing the results with the existing standard of care. If the FDA likes the data, a new treatment is born along with some new multimillionaires. Not Egorin, though. The salaried professor will keep hard at work on another trial. *—RM*

"We knew," says Jackson, "that theophylline did other things besides block adenosine, and one of the things that it did was block an enzyme called phosphodiesterase. The drugs we were using on rats blocked adenosine receptors but didn't block phosphodiesterase. We thought maybe what is going on is that theophylline has worked in the past, not because it blocked adenosine receptors, but because it blocked phosphodiesterase. We did a series of experiments to find what kind of phosphodiesterase is in the kidney and found it was a type called PDE4."

Jackson went back to his lab rats, this time treating them with a PDE4 inhibitor to see if it protected them from sepsis-induced renal failure. The answer was yes. If, like Carcillo's young patient, the rats were already in sepsis-induced renal failure and then given the PDE4 inhibitor, the answer was again yes. "If you block PDE4," concludes Jackson, "you can prevent renal failure, and you can treat acute renal failure induced by endotoxemia."

By 1996, it was time to take a stroll along O'Hara Street to Pitt's OTM and submit the five-page invention disclosure form to begin the technology transfer evaluation procedure.

Once any invention disclosure form is in the hands of the OTM, the University decides if it wants to pursue commercializing the technology. To receive the go-ahead, the intellectual property must satisfy specific criteria established by the OTM: 1) Can it be patented? 2) Does a market exist? 3) Is the inventor team committed to providing all necessary assistance? 4) How does the technology compare with existing technologies?

The OTM staff finds the answers to the first three questions. The University's Technology Transfer Committee contemplates the last question. There are no textbook answers:

"Many times it's a very difficult judgment call," says John S. Lazo, who chairs the committee and the pharmacology department. "If you had asked me a few years ago, I would never have thought that movie theaters would be places that people still go to because Blockbuster Video would have taken away all their business. And then I never would have thought Blockbuster Video would last because you could dial up on your television whatever movie you want, practically—so our ability, as an academic institution, to project into the future what is or isn't valuable is tough."

"If you had asked me a few years ago, I would never have thought that movie theaters would be places that people still go to because Blockbuster Video would have taken away all their business."

Not only is it tough, it's expensive. Every patent pursued is an expense that can total in the tens of thousands of dollars, with no guarantees. It's also time consuming. The inventor, the OTM, and outside counsel work together to draft patent claims that make scientific, legal, and business sense, building an iron-clad case for the technology. That's because a claim has a worthy adversary. "The patent office," according to licensing manager McManigle, "is doing the best that they can to narrow it." Otherwise, inventors might secure rights to future technological discoveries of others.

For Jackson and Carcillo, the University made the investment and applied for a use patent concerning the application of any drug that has PDE4-blocking activity for the prevention or treatment of sepsis-induced renal failure. After nearly two years of the expected wrangling with the patent office, it was approved.

Throughout the wrangling, the OTM was also hard at work devising a commercialization strategy. There are two options: find a company to pay a licensing fee for the intellectual property or create a company.

"In general, it's preferable to license," says Maher. Licensing avoids startup costs. However, if it makes sense to group technologies or products together for scientific, marketing, or manufacturing purposes, Maher says Pitt will not hesitate to form a "platform technology company." The PDE4 patent, along with other unrelated drug treatments, was almost the center of such a company. It even had a name—Pharmalogics. But it never accumulated enough capital to get off the ground. There wasn't much the University could do to help at that point, Maher explains:

"In the congressional debate that led to the Bayh-Dole Act, there was considerable concern that universities would fail to commercialize the intellectual property that had resulted from federally funded research. As a result, . . . the act [included] the requirement that universities not accept less than fair-market value for any intellectual property." In other words, a company able to pay fair-market value will, in Congress's opinion, have the desire and the dollars to prevent the technology from languishing indefinitely on its journey to the marketplace.

The OTM now hopes to get fair-market value for the PDE4 patent by pursuing a licensing strategy. The profit could be astronomical for a licensee, but so could the expenses. After a drug passes testing on animals, it must pass two or three more trials on humans before receiving Food and Drug

Administration (FDA) approval. Each trial can cost anywhere from $100,000 to more than $10 million, and the odds are usually no better than even that the product or treatment will ever make it to the marketplace. Considering PDE4 inhibitors' documented success with animals and that the treatment consists of benign chemicals, Jackson and Carcillo don't expect the first of two human trials to cost more than $250,000. If the treatment passes both trials and receives FDA approval, Jackson estimates annual revenue in the United States and abroad will be $200 million. Since the licensee has the most to lose, it's only fair the licensee has the most to gain, usually about 94 to 97 percent of the annual revenue. The remaining three to six percent is divvied up by the University and the inventors. Even taking into account the very real possibility that competing drug companies will find a way around the use patent, the royalties could be huge.

Such an infusion of capital could have ramifications beyond the University. Jackson, who is originally from Texas, marvels at how Austin has transformed its oil-based economy into a high technology haven that is often mentioned in the same breath as Silicon Valley or Boston.

"If we can get the biotech industry growing," says Jackson, "it will attract other players from all over the planet to Pittsburgh. We can do in Pittsburgh, through biotech, what Austin did through software." Senior officials at Pitt have such a future in mind as well. To help make this happen, the University has introduced a number of projects to get scientists to think entrepreneurially. It also has partnered with UPMC Health System and CMU to entice venture capitalists to Pittsburgh so that a few more of those well-funded companies offering fair-market value make their homes in southwestern Pennsylvania.

There are other roadblocks unique to the biotech transfer route, unfortunately. The death of Jesse Gelsinger, a teenage volunteer for a gene-transfer therapy trial conducted at the University of Pennsylvania, has university leaders, government agencies, and patient advocacy groups carefully reexamining conflict of interest issues. James M. Wilson, the Penn doctor in charge of the Gelsinger experiment, had a financial stake in the drug trial. Wilson founded the company that provided $21 million in funding for his lab, and he continued to hold 30 percent of its stock (reportedly valued at $13.5 million). Last fall, on the anniversary of Gelsinger's death, the young man's family filed a lawsuit against Penn, which was subsequently settled out of court. The tragedy has spurred federal regulators to review government agency regulations.

The Gelsinger case may appear to be a conflict of interest to some, yet Maher points out a potential Catch-22: "The difficulty a university encounters is that in the early stages of the development of a technology, it's not unusual to have the inventor be the only one in the world who can plausibly carry the project to the next step. When we find ourselves in a gray area where a desirable activity is not a clear conflict but could become one, we will generally put the project under the scrutiny of an independent committee . . . and expect [it] to protect the University and the scientists performing the research from any activities that could wander into an area of conflict."

"If we can get the biotech industry growing, it will attract other players from all over the planet to Pittsburgh."

As for the PDE4 inhibitor treatment, neither Carcillo nor Jackson anticipates conflict-of-interest concerns because the testing isn't so specialized that their involvement would be essential.

In the meantime, they wait. For a licensee, for the trials, for FDA approval, and—finally—for PDE4 inhibitors to prevent acute renal failure in patients like the young boy Carcillo watched fight for his life. That boy won his fight and walked away without chronic kidney problems. Many others—Carcillo estimates as many as 14 percent of his septic shock patients—aren't so lucky.

Like the patients and doctors, Pitt waits, too. It's certainly possible that PDE4 inhibitors may be one of the University's upcoming success stories. It's one of those technologies that is in the middle of that eight-to-10-year pipeline. Nevertheless, Pitt officials aren't penciling in future PDE4 revenue just yet. So much can still go wrong. Clinical trials aren't yet under way. And garnering FDA approval is no walk in the park. For these and other reasons, the OTM's policy is to keep its portfolio overflowing with bioinnovations. In the end, OTM officials will tell you, it's a numbers game. The more technologies that step up to the plate, the better the odds of hitting a home run. As for that promising rookie known as PDE4, it's too early to tell whether it will circle the bases.

Certainly, Jackson and Carcillo aren't quitting their day jobs.

"When my wife married me, I had nothing. I was a poor undergraduate, [then] a poor graduate student, poor postdoctoral fellow, all the way up," says Jackson, laughing. "Money isn't the driving force for me, but it would be really nice to be able to generate funds to not have to spend so much time writing grants, to have the money to go out and tell my technician, 'Let's do this crazy idea.'"

"If I wanted money," says Carcillo, "I wouldn't have gone into academics or even become a physician. What Ed and I hope to do is push the technology forward." ■

COMPANIES TO WATCH

Keep an eye on these up-and-coming biotech firms:

In search of a cure for cancer, Metacine, Inc., hopes to use the body's own cells to manipulate the immune system to destroy tumors.

CellEct Bio, Inc., is pursuing liver cell growth and regeneration.

To enable diabetics to monitor their glucose levels continuously, Sentek Group, Inc., is perfecting a noninvasive device.

And Fluorous Technologies, Inc., is devising a way to manufacture chemicals in an environmentally friendly manner.

These companies can't be found on Nasdaq just yet. They represent the most recent platform technology companies launched as a result of innovations by University of Pittsburgh scientists under the auspices of Pitt's Office of Technology Management (OTM). For now, none of them employs more than 10 people and none has a product currently available, but according to OTM officials, within the next decade it's likely that any one of them could be a breakout company with 100 or more employees and publicly traded on a major stock exchange. —*RM*

Housing in the vicinity of Pittsburgh's new highway, June 1950.

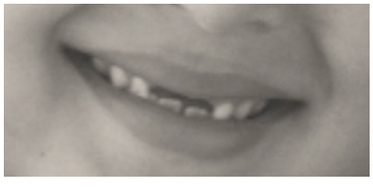
HERB NEEDLEMAN TOOK ON THE DISEASE OF WHERE WE LIVE AND WORK | BY REBECCA SKLOOT

HOUSES OF BUTTERFLIES

After Frank Durr died in a straightjacket in 1924, workers at the DuPont Deep Water plant thought they knew what killed him. They figured it was the same thing that killed William McSweeny—whose sister called the police for help after he went home sick from his work at a similar Standard Oil facility, then woke up the next morning violently insane. He died in a straightjacket, too. Fifteen others did as well, and the dead men shared one more feature: They all had worked in a House of Butterflies—a building for tetraethyl lead synthesis—so named because its workers were known for brushing hallucinated insects from their bodies.

In the early 1920s, in an attempt to outdo Ford's Model T, General Motors mounted efforts to find an agent that would quiet the Cadillac, whose knocking engine kept it lagging in popularity. What they came up with—an old compound Germans had developed called tetraethyl lead—silenced knocking engines and inspired a burgeoning new product: Ethyl Gas. But shortly after mass production of leaded gasoline had begun, workers in Deep Water, New Jersey, and at two other plants started developing a mysterious and often fatal illness. New York and New Jersey responded quickly, banning leaded fuel and ceasing its production at the plants, but their action was only temporary. After a six-hour Surgeon General's meeting, the ban was lifted, production resumed, and lead soon found its way into everyday use, fueling more than half a century of heated debate.

Twenty-five years after the deaths of Durr, McSweeny, and others, the 2 p.m.-break whistle echoed along the Delaware River behind Deep Water, and Herbert Needleman filed out with the other workers. Needleman, a second year medical student at the University of Pennsylvania paying his way through school, had soaked through his clothes in the plant's heat, which usually topped 100 degrees by early morning. He peeled off his elbow-length rubber gloves and headed outside for a cigarette. Every day when the break whistle blew, Needleman and



PHOTODISC

PHOTO OF GIRL | LISBOHN, CARNEGIE LIBRARY
PORTRAIT OF NEEDLEMAN | FRANK WALSH

other men would swarm across a field, far from the plant and its explosives, into wooden smoking shacks with glowing cigar lighters embedded in the walls. There, Needleman would smoke and check out his coworkers. In the corner, a few older men sat staring blankly into space, moving slowly and clumsily. If they spoke, their voices were distant and empty. One day, when Needleman asked other workers the story behind these men, they all shook their heads. "Oh yeah," one told him, "those guys worked in the House of Butterflies."

Needleman joined the University of Pittsburgh School of Medicine in 1981, leaving Harvard University to join Pitt's Departments of Psychiatry and Pediatrics. Calling professor Needleman a leader in the field of lead research would be an understatement. (The champion of preventive medicine has long since kicked the smoking habit, by the way.) He has spent much of his career attempting to convince others that exposure to lead, even at low doses, has tragic effects on individuals and society. Though few deny that high doses of lead are toxic, its low-dose effects have been passionately debated. If you ask Needleman where arguments against the danger of low-dose lead exposure come from, he'll tell you it's the lead industry—an entity he has fought through several turbulent decades. The battle starts with Needleman's first academic paper, and spans through scientific misconduct charges brought against him (by researchers who served as paid expert witnesses for the lead industry), to his work today.

As for the scientific misconduct charges, the committee that investigated him regarding the allegations directed Needleman to correct and clarify published reports of certain methodological aspects of his work and to make available to any interested scholars his complete data set on his tested subjects. More importantly, the committee asserted that the conclusions from his data were robust. Needleman had not engaged in scientific misconduct. Further, his early findings on subclinical lead exposure have since been confirmed by similar studies in Australia and elsewhere. And his efforts to de-lead America in the name of public health, even in the face of scalding controversy, have won him prestigious honors such as the Dana and Heinz Awards.

As for halting the effects of low-level lead exposure, Needleman has had a few victories, but at 73, it's a fight that still consumes him.

Rubbing his eyes gently, Needleman lets out a deep sigh when he talks about lead and its effects. "Lead does so many things to human biology, we don't even know which ones are most important," he says. It affects neurotransmitters responsible for nerve conduction, causes leaky capillaries, kills brain cells, affects RNA transferase and transcription of the genome, and that's just an abbreviated list. "There are thousands of articles out there," he says, "and so many effects that could be critical, we don't really know what's what," and then he pauses. "We just know that the more you look for brain effects, the more you find them, even at very low doses."

Needleman recalls how in 1960, according to the Centers for Disease Control and Prevention, a child needed at least 60 micrograms of lead per 100 milliliters of blood to be officially identified as poisoned. Back then, 20 percent of inner city children had blood lead levels of 40 to 50 micrograms per 100 milliliters, and they were considered normal. This made no sense to Needleman. *Listen,* he said, *if we know for a fact that high-dose lead poisoning causes obvious problems—like coma, retardation, and death—why should we assume that lower levels cause no injury to a child's brain?* He has asked this question repeatedly for about five decades. Almost every time he does, he designs a study to examine it from a new angle. (Today, the toxic lead level is defined as 10 micrograms per 100 milliliters, and still 21 percent of inner-city children have lead levels above that, according to Needleman.)

In the '70s, Needleman's community mental health office was what used to be a living room in an old brownstone in an impoverished section of Philadelphia. Each morning Needleman stared through his office window into a primary schoolyard across the street. It was full of poor kids, mostly minorities, who lived in turn-of-the-century houses with peeling lead paint. As they giggled and ran by his window, Needleman started to think to himself, *How many of those kids aren't going to make it because they are lead poisoned? And what other damage might they suffer from lead's toxins?* To find out, first he needed a better measuring stick. Lead is a bone-seeker—like calcium, it migrates into bone, where it accumulates. So if a child were exposed to lead during, say, the first three years of life, a blood-level test at four might not show any lead. At the time, the only accurate test of long-term lead exposure was a bone biopsy, which would not have been acceptable for hundreds of seemingly healthy children. But when a child loses a tooth, Needleman realized, it's like a spontaneous, pain-free biopsy. He got a $500 grant from the federal government, took a chunk of it to the local bank, and converted it into silver Kennedy half-dollars. Then he had little badges made up that said "I gave." With his half-dollars and badges, Needleman worked with the schools to collect teeth from several locations—some from Philadelphia's "lead belt" on North Broad Street, a hot spot for poisoning, others from areas that rarely reported lead poisoning. Those teeth, Needleman established, were good markers for lead levels.

That got him an invitation to Harvard, where he would show the world lead's subtle destructive powers. In 1979, in a study on Massachussetts children, he determined their life-long accumlation of lead and examined whether that correlated with their IQs. He found that children with higher accumulations of lead also had, on average, five or six fewer IQ points than those from the same neighborhood, ethnic background, and economic status with lower accumulations.

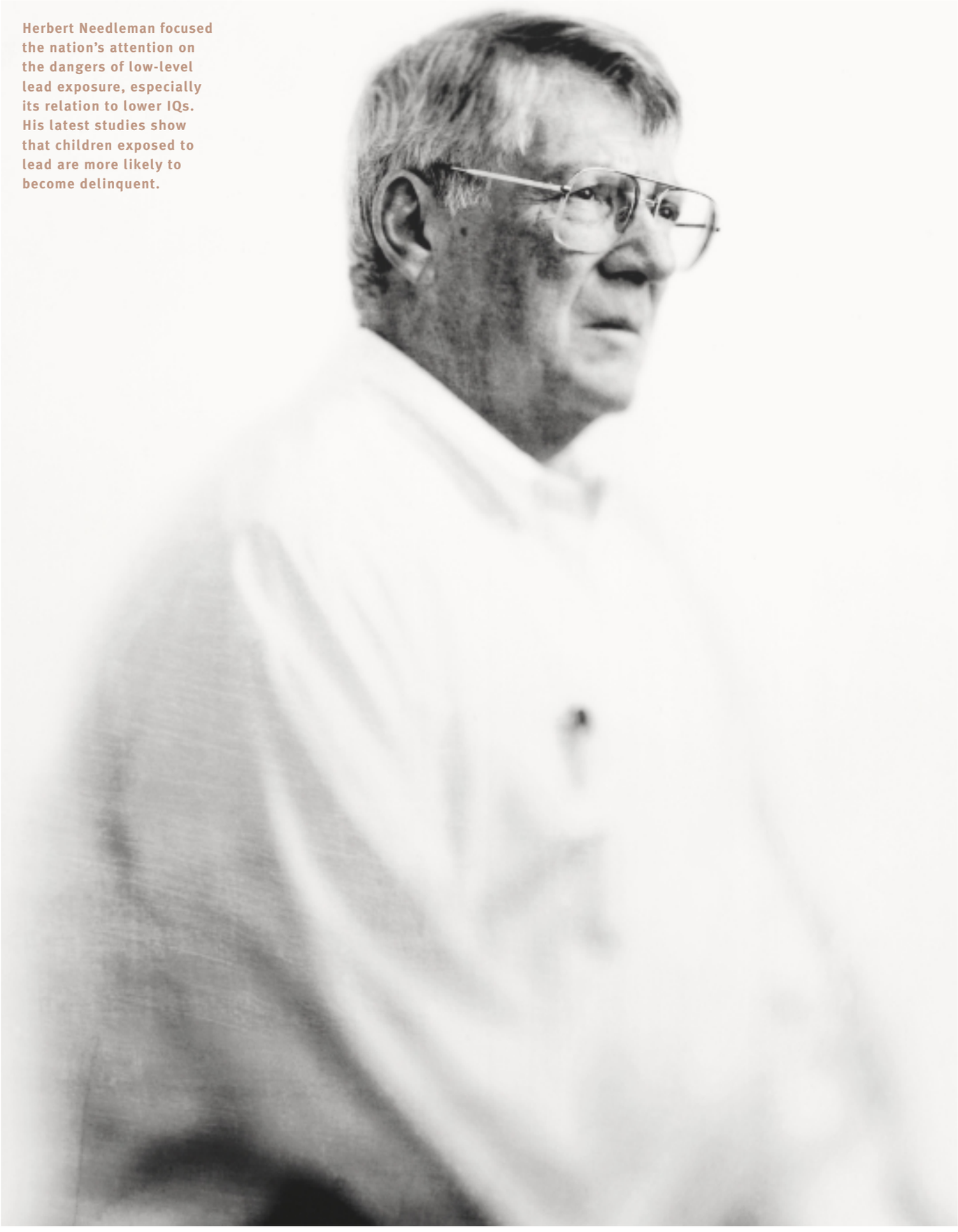
"That study," says Philip Landrigan, professor and chair of community and preventive medicine at Mt. Sinai School of Medicine, in New York, "really changed the whole way the world thinks about lead poisoning."

"He really made the world consider the possibility that subclinical exposure to environmental pollutants could have a serious societal impact," notes David Bellinger of Harvard Medical School, who has collaborated on studies with Needleman.

"These low-level exposures may not result in a child who is clinically ill, but he showed that there is a more subtle impact: It reduces the child's quality of life, and when the effect of lead is projected across the whole population, it has a cumulative impact that's really substantial. It's shifting the whole distribution of cognitive level a bit toward the lower end." Needleman calls this the subtle dumbing down of America; he doesn't take it lightly.

"Her disease was where she lived, and why she was allowed to live there."

When people hear the story of Needleman working at Deep Water and seeing lead-poisoned workers from the House of Butterflies, they are likely to say, *Oh, that explains why he's anti-lead.*



Herbert Needleman focused the nation's attention on the dangers of low-level lead exposure, especially its relation to lower IQs. His latest studies show that children exposed to lead are more likely to become delinquent.

But actually, it doesn't. For Needleman, the significance of that day at Deep Water did not hit him until years later, after an experience with a young Hispanic girl changed his understanding of lead poisoning and its causes.

It was the early 1960s, Needleman was a self-proclaimed "cocky" resident at Children's Hospital of Philadelphia, and a young girl, we'll call her Vanessa, was admitted to his ward with severe lead poisoning. She had eaten the lead-based paint peeling from her inner-city home, and her story was all too common. Her brain had swollen to a point where she was dangerously near death. She didn't cry, didn't smile, just lay there, comatose. Needleman treated her with EDTA, a chelating agent and the only drug available to counter lead poisoning. Soon, she woke up crying, and Needleman breathed a small sigh of relief. Within a few days, she smiled the sweetest smile Needleman can remember. He felt proud, even smug. When he knew the girl was going to make it, he turned to her mother and calmly told her she had to move from her home.

"If Vanessa eats more paint," he said, "there's no question she'll be brain damaged."

Her mother shot Needleman an angry look and snapped, "Where can I go? Any house I can afford will be no different from the house I live in now."

Needleman's smugness vanished. "I realized," he says, "that it wasn't enough to make a diagnosis and prescribe medication. I'd treated her for lead poisoning, but that was not the disease—the disease was much bigger and caused by forces embedded in the child's life. Her disease was where she lived and why she was allowed to live there."

Historically, childhood lead poisoning has been a problem for minorities and low-income families. "There's much more lead in poor, black, and Hispanic neighborhoods because of the kinds of houses they live in," Needleman points out. "There are middle-class white kids who are affected, but the rate is five to six times higher in the poor neighborhoods." Today, old paint is the most important factor, but for several decades, lead in gasoline compounded the problem. After the deaths at Deep Water and other plants, there was a brief moratorium on leaded gasoline. Soon after though, lead became a major component of everyday life in America, most notably as an additive to gasoline and paint. In 1973 alone, as Needleman puts it, "200,000 tons of lead were blowing out of the exhausts of American cars each year." He thought this was a crime. The more studies he conducted, the more deleterious effects from lead he found. Through governmental committees, editorials, and other means, Needleman and other researchers fought against leaded gasoline for 40 years.

"Dr. Needleman was a key figure in persuading the Environmental Protection Agency to take lead out of gasoline," says Landrigan. "That single action of taking lead out of gasoline has brought a 90 percent reduction in blood lead levels in children of this country."

Needleman wants to do the same for leaded paint. He says, "See, if you de-lead a house, that house is safe forever. It's not just the kid who's living there you're protecting—it's any kid who moves in. And in the poor neighborhoods, during the lifetime of that house, there may be 10 different families in there, so you're protecting all those children." Then he pauses.

"Dr. Needleman was a key figure in persuading the EPA to take lead out of gasoline. That single action . . . has brought a 90 percent reduction in blood lead levels in children of this country."

"In a way," he whispers, "it's a bargain.

"People say we can't afford to do it. We can't afford not to do it. The actual cost-benefit analysis done by the Public Health Service shows that, in terms of avoided health costs and special education fees, there will be a $28 billion savings for de-leading all the houses. So there are a lot of good reasons to do it: moral, ethical, and practical reasons."

When moral and ethical motivations are involved, it seems Needleman will go to any lengths to right a situation, and it's not unlikely for him to upset a few people along the way. As an antiwar activist during the Vietnam War, for example, he traveled overseas to rescue wounded Vietnamese children and bring them to the United States for medical care. He and Benjamin Spock, the famous pediatrician who was a mentor for Needleman, spent their share of time together, including one night in jail for an antiwar protest. During all of this, Needleman kept up his fight against lead.

While at Harvard, Needleman studied newborns, taking blood from umbilical cords to determine prenatal lead exposure. He found that even at very low doses, infants born with higher lead levels had slower neurobehavioral development than those from the same backgrounds with less exposure in the womb.

Later, at Pitt, Needleman and his colleagues reexamined kids from the famous Harvard IQ study that he had conducted 11 years earlier. Those kids, at 17- or 18-years-old, were more likely to be dyslexic, drop or flunk out of high school, and get arrested if their lead levels surpassed 10 micrograms.

Most of the lead studies to date, including Needleman's, have focused on IQ, but he doesn't think that's the most important factor. "I think lead affects attention, behavior, and impulsivity," he says, quickly pointing out that this isn't a new idea. Another mentor, Randolph Byers at Children's Hospital in Boston, first saw this connection in a few patients referred to him for aggressive behavior during the '40s. But Needleman is the first to explore this connection through in-depth studies.

In 1996, Needleman conducted his first delinquency study; it involved several hundred children. He measured their bone lead levels and collected reports of aggression and delinquency from the subjects, their parents, and their teachers. With this study, Needleman showed an association between lead and delinquency. For him, the next logical step was to see if lead affected arrest rates. He identified about 200 adolescents who'd been sentenced to time behind bars and a control group of teens from local high schools with no arrest records. He measured the lead stored in their bone, using a relatively new non-invasive technique called X-ray fluorescence spectroscopy, and found that, controlling for race and socioeconomic class, mean lead levels in delinquents were significantly higher.

"Well," he says with a tisk, "that's a lot of delinquency. And the thing about lead toxicity is, it's completely preventable." He shakes his head. "Of all the causes of delinquent behavior, this is probably the easiest one to get at. If you just take lead out of the houses, then people won't get poisoned, and a significant amount of delinquency might well disappear. Just think of what that would do for our society."

"Lead, as Herb has said so many times, is a simple problem," says Bellinger. "We know where it is, how it gets into the body, and the damage it can do. In some ways, it's a bellwether of our abilities as a society to address these problems." ■

People and programs that keep the school healthy and vibrant

THE PRICE TAG FOR EXCELLENCE

CAMPAIGN ANNOUNCED

BY ROBERT MENDELSON

On paper, there were many reasons why Matthew Hayn was an outstanding medical school applicant for the Class of 2003. He would graduate *magna cum laude* from Muhlenberg College, in Pennsylvania. His MCAT score surpassed the 10.5 average of Pitt's incoming medical students. He had always been an active community volunteer. In addition, Hayn sang in Muhlenberg's choir, cocaptained its cross-country team, and helped secure a national charter for his fraternity.

Well-rounded credentials. But for an 8-year-old named José, credentials meant nothing. After enduring a five-hour bus ride from his home in Connecticut to a summer camp in the middle of New Hampshire, little José didn't need an ambitious premed as his counselor. He needed a shoulder to cry on.

"He was really homesick," recalls Hayn, who was the boy's counselor in 1996. "During the day, he was fine. When kids are running around playing, they don't think about how much they miss Mom."

Nighttime was a different story. "I would take him outside and try to cheer him up and remind him how much fun he was having."

After awhile, José wouldn't feel so bad. "I'd give him a hug and send him back in the cabin," says Hayn.

By the end of José's stay, Hayn noticed his new friend had become more outgoing. The next summer, Hayn was back at camp. So was José.

This time, he came back for two weeks instead of one. And he wasn't homesick. Near the end of that second summer of camp, José sought out Hayn. "He just wanted to thank me for being his friend the year before and for giving him the hugs."

Not only did Hayn excel academically, but he clearly excelled in helping people. When it came time to apply for medical school, the real question was what school wouldn't want him. Pitt certainly did. So did others.

"Pitt and Columbia were sort of neck and neck as my number one choice," he says. As they neared the homestretch, Pitt made its move. "I was just about to arrange a second meeting with Columbia . . . " says Hayn, "when I got a telephone call from Pitt." It was from the Medical Alumni Association: He had been awarded a merit-based scholarship that would pay nearly half his tuition.

That was good news. The son of a Lutheran minister, Hayn describes his financial situation as "typical middle class," which made the expense of a medical education daunting.

After telling Hayn the news, the caller said, "So, I assume you will be going to Pitt?"

"At that point," says Hayn, "I was still waiting on Columbia, but I really did like Pitt." He said yes, then and there.

In order to have more Matthew Hayns choose Pitt, the medical school plans to create more scholarships. In fact, it's one of three top priorities the school has outlined as part of the $500 million Campaign for the University of Pittsburgh, announced last fall during Pitt's Discovery Weekend (see page 38). Lawrence D. Ellis, MD '58, professor of medicine, and Freddie H. Fu, MD '77, chair of the Department of Orthopaedic Surgery, are cochairing the school's effort to raise funds.

The school's two other campaign priorities address equally critical issues for Pitt, as well as the nation's health. Commentators throughout the country are wondering who will serve as the next generation of physician-scientists—men and women who not only teach but bring a vital perspective to biomedical research. It has been difficult to attract bright med students like Hayn to careers as scientific investigators. Postgraduate training, especially when it means delaying income as a physician, is an expensive proposition. To combat this, Pitt hopes to identify, nurture, and help fund a new generation of Jonas Salks and Thomas Starzls.

The remaining priority—to establish the Center for Human Genetics and Integrative Biology—will position Pitt well to reap the fruits of the Human Genome Project. The school will recruit top scientists to staff the center. And faculty throughout the school will be able to turn to the center for support as they investigate the many roles genetics plays in our well-being and uniqueness.

TOP: Matthew Hayn, MD '03
LEFT: Larry Ellis, MD '58, (seated) and Freddie Fu, MD '77, are leading the school's capital campaign.

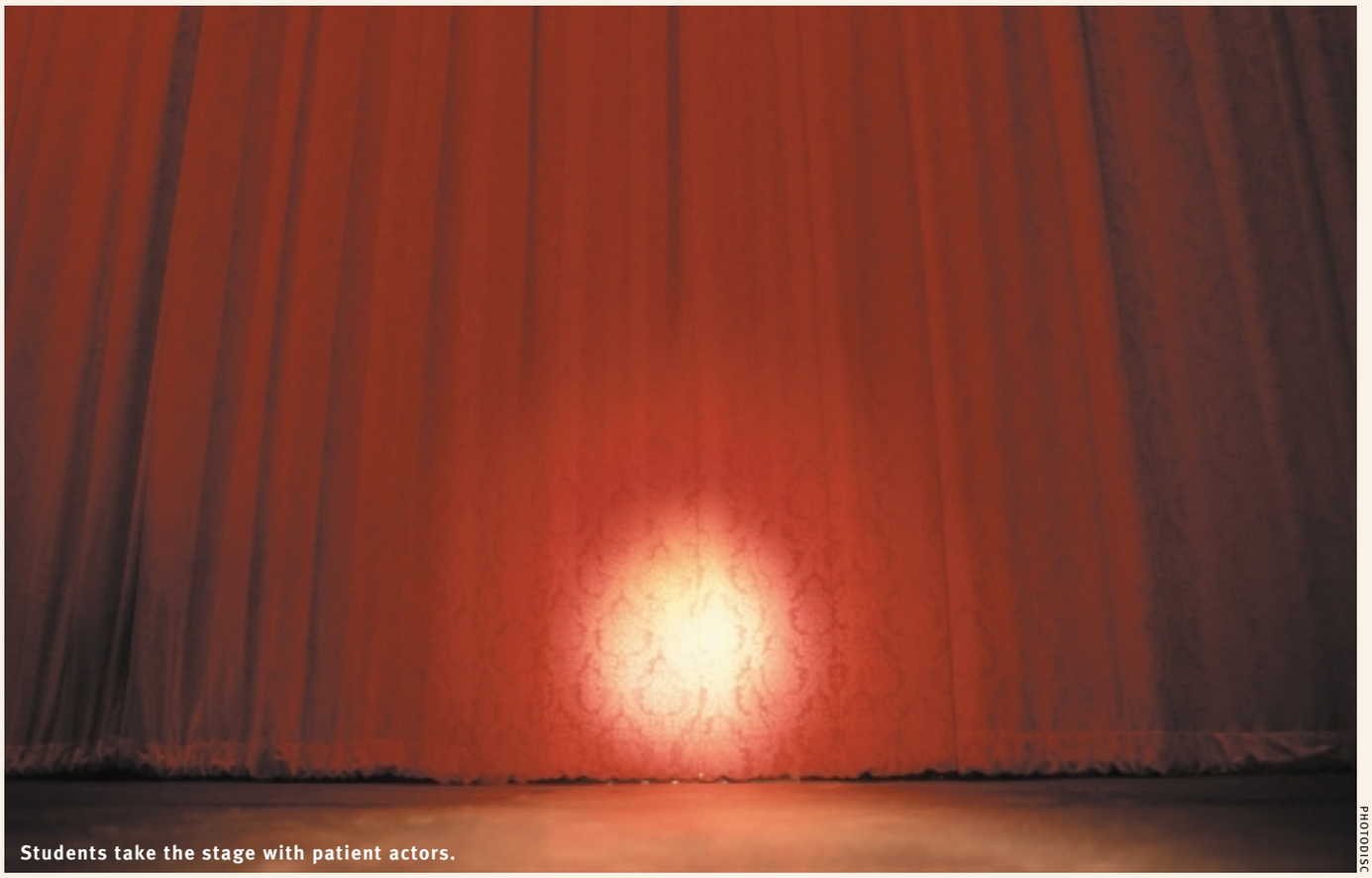
Say an investigator doesn't have the equipment, or perhaps the expertise, to run tests that will help expand the parameters of her research. She will be able to tap into the center's staff and core labs. "Without those core labs," says Michael Gorin, the center's interim director, "it's sort of everyone for themselves."

The center also will serve as a resource for physicians and patients. Its Internet site will post course modules on genetic diseases for patients and their families and help physicians track patient tests and other important records.

As Fu and Ellis spread the word of the campaign's three priorities, they should expect to find sympathetic ears. "When we tell people what this money will be used for," notes one advancement official, "it makes it hard for them to say no." ■

ACT ONE

IN THIS SCENE, STUDENTS TREAD DICEY TERRITORY | BY DOTTIE HORN



Students take the stage with patient actors.

PHOTODISC

Stephanie Sterrett, a first-year medical student, wonders if she will be able to establish rapport with her patient, Randall Lee, a wiry man with graying hair, a Baptist who doesn't drink or smoke, a 59-year-old owner of a construction business.

Actually Lee is not a real patient, but an actor playing a role; he sits alone at the front of a small room in the University of Pittsburgh School of Medicine's Scaife Hall. Sterrett approaches him and, in lieu of a door, knocks on a table, around which her classmates are gathered. Several of the students have already interviewed Lee, each building on the information gathered by the others. She sits down and explains to Lee that she knows about his occasional symptoms—numbness, a vibrating sensation in his abdomen, and increased gas. "Have these symptoms been worrying you lately?" she asks.

"As they continue, yes," Lee responds in a slow, Southern drawl.

"Has this impacted your life in any way?"

"No, I'm pretty busy."

In this first-year Patient Interviewing Course, students spend most of their time interviewing "simulated" patients. The seven-week course allows students to practice skills essential to taking a patient's history, such as gathering accurate, detailed information, fostering patient openness and trust, and responding to a patient's emotions, says Laurel Milberg, course director. "It's trial and error, experiential learning," she says. "The goal is practice, practice, practice."

Sterrett asks Lee if he has any idea what is causing the symptoms, and if he has talked to anyone about them. "Are there any other problems you've been having with your health lately?" she asks.

"Well, I did, probably in March, see a doctor," Lee says. "I found that when I would urinate, I would get this sort of ache at the base of my penis, and I noticed that, there was some, would appear to be some form of dribbling." Lee tells how he visited a physician friend who said the problem had to do with his prostate; the friend prescribed a drug that cleared up the symptoms.

Sterrett calls a time-out to seek advice. "I don't know where to go," she says, her voice full of high-pitched energy.

"It seems a little sketchy, 'cause he saw his friend. It doesn't sound like he actually figured out what it was," says a classmate near the front of the room.

"I would go a little more into the prostate thing," adds another.

"He tells you something which may be a sexually transmitted disease, and what are you thinking about?" asks Paul Needle, an instructor for the course.

"Oh, no," Sterrett says. The room fills with laughter. Now everyone is talking at once. The discussion turns to ways to raise sexual issues with Lee.

"Well, say, *How is your marriage?* And then go to, *Are you having any problems with your marriage?*" offers one.

"I am just really blunt, and I'm just afraid I'm going to offend him," Sterrett says.

"Do it in a way that's comfortable for you," Needle says.

Sterrett ends her time-out. She asks Lee if he is away from home a lot on business. She builds up to her question delicately: "Did you have other sexual partners while traveling?"

"Oh, ah, hah. Let me make it very clear that I am a Baptist, and I would never, ever have a relationship with another woman outside of my marriage. No, no. The answer to that is no."

Needle calls a time-out to make a point.

"What was his answer to your question? What were his words?" Needle says.

"Relationships with other *women,*" Sterrett says, laughing softly.

"But, if he's a Baptist, maybe it doesn't even occur to him to like, acknowledge that," posits a classmate, referring to homosexuality.

Sterrett cringes at the thought of broaching the subject. "Well, how am I going to ask him?"

"Have you ever had sex with a man?" Needle offers.

"Yeah, but, I think that'd be like starting a fight," objects a classmate. "He just said, I'm a Baptist."

"He said, I want to make this very clear," another student says in agreement.

"We're talking about getting a chance to practice something which is uncomfortable, and therefore valuable," Needle says.

"Okay, so this is my last question, and then I'm done?" Sterrett says.

"Maybe," Needle says.

"Unless something interesting comes up," Sterrett says.

"Go, Stephanie," an encouraging voice from the class says softly.

She turns back to the patient. "Mr. Lee. You said you had not had a relationship with another woman. Has there ever been a time when you ever had any relationships with other men, either before your marriage or during it?" she says.

Lee looks at his lap and doesn't answer.

Sterrett is silent. A good half-minute ticks by, but she doesn't push him.

"Well, the answer is yes," Lee says, rubbing his palms across his eyes. "I've only had three experiences. It's happened once a year for the last three years. I seem incapable of stopping it. I fear, I fear that these symptoms may have something to do with something like AIDS or something."

"We can find that out," says Sterrett. They discuss his fears. She ends the interview.

"Wow. That is not even something I would have even picked up on. That was pretty much the whole main reason for his being here," Sterrett says. "He could easily have lied and denied it, but I think he wanted to get it out."

Needle encourages her to find out more about the thoughts of this character, "Randall Lee." The actor, Bruce Hill, a Pitt drama instructor, is still in role. Out of a sketch of a man—traits, symptoms, and psychosocial issues—Hill has developed Lee into a full-fledged character; he knows his thoughts, feelings, reactions. Sterrett asks Lee if he was gratified to speak.

"The truth is that I've been to other doctors, and I've wanted to discuss it, but I've not been able to," Lee says. He reveals his desire to talk and his fear. "Just by sitting there and being quiet, you let me reach my own decision," he says. "It made it easier." ■

"He tells you something which may be a sexually transmitted disease, and what are you thinking about?"

METHOD PATIENTING

"No death or dying or major anger," urges Kenneth Gargaro.

Gargaro, a theatre director, trains actors to be simulated patients. He is giving a pep talk to 16 actors, who will portray patients for first-year students in today's Patient Interviewing Course. In the next couple of weeks, Gargaro's cast will "have" a gamut of illnesses, including stroke, panic disorder, diabetes, lupus, and gastrointestinal bleeding. Today, however—no matter how inspired the actors may be—death and dying and major anger will *not* emerge as issues with which the patients are grappling. *That* happens in the final two weeks of the seven-week course. For today's class, week five, emotions surface as the student interviews the patient, but they are relatively mild—suspicion that symptoms may mean a serious illness, embarrassment over sexual matters, resentment about having to speak to a young medical student. The students learn to respond to less-intense emotions before tackling the severe ones.

"The students need to identify that emotion, they need to understand it, they need to respond empathetically," says Gargaro. *—DH*

PERSON TO PERSON

THE NATION'S FIRST CHAIR IN PATIENT CARE

BY ROBERT MENDELSON

ARMAND WRIGHT

Robert Arnold

The prognosis for the 83-year-old man is bleak, and he's thinking, again, about what that really means. When his wife came in this morning, she left with him a brand new photo of his great-granddaughter, which he holds in his hand now. She is kneeling with a soccer ball, flashing a big grin. He adores that little girl, but probably, he's never going to see her play a game. In a few years, maybe she won't even remember her great-grandpa. His wife tells him it's awful to think such things, but he can't help it. He turns the photo over and places it on the edge of his bed. He's tired.

He doesn't notice that his doctor has walked into the room. It appears that the doctor hardly notices him either: His eyes are focused on a medical chart.

"I need to ask you a few questions," the doctor informs him. "If your heart stops, do you want us to restart it, and if your blood pressure gets low, do you want me to put you on medicine to raise it?"

The patient has no answers, only questions. Is he about to die at any moment? Has the doctor given up on him? Should he give up on himself?

Robert Arnold will tell you that this scenario could, and should, have gone differently.

Arnold, who is a professor of medicine at the University of Pittsburgh School of Medicine, suggests another way the physician might have broached these end-of-life issues: "What if the doctor had said, 'What are your concerns and fears? When you think about the future, what do you think about?' I think the doctor would have had a very different discussion with that patient."

It's this kind of dedication to a more meaningful and humane dialogue that led to Arnold's appointment last July to the Dr. Leo H. Criep Chair in Patient Care. The chair's namesake, who died in 1992, taught at the University of Pittsburgh for 50 years and was the chief of medicine at UPMC Montefiore and a renowned allergist. Arnold knew him personally. "He was very beloved by his patients," says Arnold, "and very interested in both doctor-patient communication and doctor-patient relationships and the influence each has on medical care. He was concerned a great deal about how the transformation of medicine through technology might undercut that relationship."

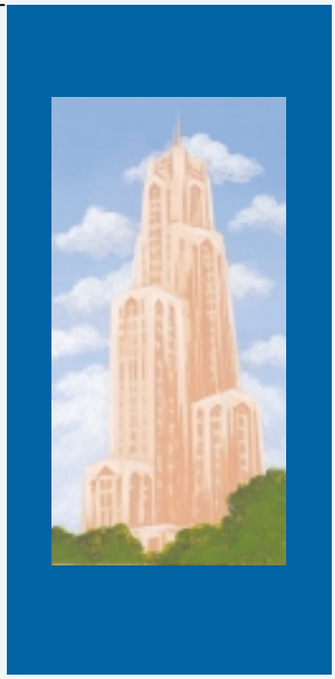
Hence, the Criep family worked with school officials to create what is believed to be the first endowed chair in a medical school with a mission to nurture the multi-faceted connection between doctors and patients.

The kinds of difficulties patients and their families go through made an impression on Arnold himself when he was just a boy. His older brother had leukemia and died when Arnold was about 5-years-old. "I don't remember very much about the doctors," he says. He remembers the hurt, however; his eyes well up at the mere mention of the heartache. That's when Arnold started thinking about becoming a doctor.

After high school, he enrolled in the University of Missouri's six-year medical school program. He majored in philosophy because, in part, he says, "the biology and chemistry courses were boring." During his freshman year, he took a course in medical ethics and was intrigued by the issues it raised. Today, it's part of his job to make sure Pitt's curriculum addresses such topics.

Lessons about doctor-patient communications—which could focus on issues as seemingly simple as learning to listen—aren't taught with lectures. Through discussions of cases like the elderly man being questioned about end-of-life measures, Arnold hopes to instill skills that have little to do with a scalpel: "Some may view what I teach as common sense. Anybody can talk. But the truth is, we're not very good at talking to each other."

When it comes to matters of the heart, there are no right answers. Yet, notes Arnold, "The fact that there is no right answer does not mean there are not wrong answers." ■



CLASS NOTES

'50s

HENRY J. MANKIN, MD '53, professor of orthopedics at Harvard Medical School, was the speaker at the inaugural Marshal S. Levy, MD, Memorial Lecture given in Pittsburgh last fall. Mankin and Levy were classmates at the School of Medicine.

CYRIL H. WECHT, MD '56, has been honored by Duquesne University, which has established the Cyril H. Wecht Institute of Forensic Science and the Law. The institute is designed to inform health care professionals, among others, about the emerging role of forensic science both in related fields and in the judicial process.

'60s

FRED F. CIAROCHI, MD '69, is president of the Dallas County Medical Society. Last spring, he led the University of Texas Southwestern Medical School Class of 2000 in reciting the Hippocratic Oath.

'70s

HOWARD K. RABINOWITZ, MD '71, has been elected to the Institute of Medicine. Institute members engage in a broad range of studies on health policy issues. Rabinowitz is a professor of family medicine at Jefferson Medical College in Philadelphia, Pennsylvania. He also directs the Physician Shortage Area Program, which works to increase the number of family doctors in rural and other underserved areas.

'80s

MICHAEL D. PATTERSON, MD '80, is chair of the Department of Medicine at Mercy Providence Hospital in Pittsburgh.

A. KIMBERLY (POPOVICH) IAFOLLA, MD '84, has been appointed medical director of the Adventist Center for Children at Shady Grove Adventist Hospital in Rockville, Maryland. She also chairs the institutional review board of that hospital. She can be contacted at kiafolla@aol.com.

'90s

STEPHEN GILMAN, MD '91, is an assistant professor of psychiatry at New York University School of Medicine. He also is a consultant to the Hazelden Foundation and in private practice in New York City, where he specializes in addiction psychiatry as well as corporate and workplace wellness. He can be reached at gilstep2@pol.net.

LARA J. KUNSCHNER, MD '94, a neuro-oncologist, has joined Allegheny General Hospital in Pittsburgh, where she will serve as medical director of that hospital's neuro-oncology program. She completed her neurology residency at the University of Michigan and a fellowship in neuro-oncology at the University of Texas.

***The Owl*, 1953**

CATHY NELSON-HORAN, MD '97, has graduated from the emergency medicine residency program at Grand Rapids, Michigan's Spectrum Health Downtown (formerly Butterworth Hospital) and is on the full-time EM faculty at Hershey Medical Center in Hershey, Pennsylvania. —*RM*

REUNIONS

Evidently few among the **CLASS OF '75** have cholesterol concerns. At least not among those who attended their 25th reunion on November 4. At the dinner—held at the Top of the Triangle, which overlooks downtown Pittsburgh—doctors could choose either tenderloin or salmon for their entrée. Few chose salmon, according to class agent Barbara Zawadzki, MD '75, who organized the affair. One favorite topic of discussion was the free-spirited mode of transportation of Charles Kelley, MD '75. Kelley informed everyone he still rides his motorcycle regularly, and he had one other bit of information. He was retiring from his thriving pediatric practice.

As for the future, he and the rest of his classmates in attendance were already discussing their next reunion in 2005. —*RM*

WEEKEND EDITION

Extra! Extra! Pitt unveils a $500 million capital campaign; more than $350 million already raised! That was the BIG news on campus during the last weekend of October, dubbed Discovery Weekend. Among the flurry of activities, **CATHERINE DEANGELIS**, MD '69, editor of the *Journal of the American Medical Association,* and **BERNARD FISHER**, MD '43, returned to Scaife Hall as "Legacy Laureates." Speaking at Grand Rounds, Fisher chronicled his groundbreaking breast cancer research. In his opening remarks he noted, "It's important that a new generation of students and faculty of this institution realize that for 40 years there were a large number of people on the ninth floor of Scaife Hall who planned and conducted research that led to the radical and revolutionary changes that have taken place in both the understanding and treatment of breast cancer."

At the conclusion of his remarks, Fisher received a standing ovation.

ARMAND WRIGHT

ABOVE: Bernard Fisher (MD '43) BELOW: Karen (MD '86) and Doris Rodman

Doris Rodman and her daughter **KAREN RODMAN**, MD '86, didn't receive a standing ovation for their role in Discovery Weekend. That doesn't mean they didn't deserve one, too.

Karen Rodman's journey to Pitt began when she was 8-years-old. She had lost her father three years earlier, when he died suddenly from a heart attack. Now her mother was being whisked away from their home in Virginia, to undergo major surgery in New York. The little girl worried she was about to lose her mother. Four weeks later, she came home from school, and there was her mom waiting at the door.

"She looked wonderful," says Karen Rodman, who became enamored with medicine at that very moment and is now a neurologist in Indianapolis. The Pitt med grad and her mother fear the spiraling costs of medical education could dissuade others from pursuing similar dreams. For that reason, they announced during Discovery Weekend that they are establishing a scholarship for minority students at the school.

As the campaign continues, look for more big news from the medical school. —*RM*

RAYMOND E. MASTERS
JANUARY 23, 1910–AUGUST 16, 2000

Weekly rounds for the late Raymond E. Masters, MD '35, differed from those of his colleagues. He didn't walk the halls of a hospital, recalls his classmate and widow, Ruth Snyder Masters, MD '35. Instead, he wove a path through Bettis Laboratory, in western Pennsylvania, in his capacity as medical director of the nuclear technology facility. The health of more than 5,000 employees depended upon Masters's expertise in identifying potential health hazards. He did his job so well the Atomic Energy Commission chose him in the late '40s to help establish radiation health safety rules, many of which are still in existence today. He served as medical director of the laboratory for more than 35 years, before retiring in 1975. —*RM*

Raymond E. Masters

Robert and Jean Swope Nickeson

ROBERT W. NICKESON
JULY 1, 1921–OCTOBER 12, 2000

Of course, the parents of the late Robert W. Nickeson, MD '43, had many reasons to be proud. Their son was a well-respected physician. A published medical historian. He excelled in tennis and music, even served as president of the Mendelssohn Choir of Pittsburgh. To his parents, all of those accomplishments must have paled in comparison to his chosen specialty: ophthalmology. Nickeson's parents were blind, and, according to his wife, Jean Swope Nickeson, he needed no further motivation. Nickeson was chief of eye service at Allegheny General Hospital and conducted free clinics at the Eye and Ear Hospital for several decades. He also loved to write and contributed to many School of Medicine alumni publications. Many alumni came to know and befriend him through those stories. —*RM*

IN MEMORIAM

KARL B. CHRISTIE (MD '53)
OCTOBER 9, 2000

NANCY M. DICOLA (MD '49)
OCTOBER 3, 2000

GERALD P. DURKAN (MD '49)
AUGUST 19, 2000

IRVING F. ERLICHMAN (MD '44)
JANUARY 9, 2000

DONALD G. FERGUSON (MD '46)
AUGUST 28, 2000

ROBERT A. HEINLE (MD '59)
AUGUST 1, 2000

RAYMOND E. MASTERS (MD '35)
AUGUST 16, 2000

MARTHA SCHICK MEREDITH (MD '47)
JULY 24, 2000

JOHN A. MURRAY (MD '58)
OCTOBER 3, 2000

KURT J. NELLIS (MD '83)
SEPTEMBER 29, 2000

ROBERT W. NICKESON (MD '43)
OCTOBER 12, 2000

PHILIP B. O'NEILL (MD '41)
SEPTEMBER 16, 2000

JAMES S. RANKIN (MD '49)
AUGUST 27, 2000

JEROLD R. RUBEN (MD '55)
AUGUST 9, 2000

MENDEL SILVERMAN (MD '46)
SEPTEMBER 16, 2000

JOHN S. WITHERSPOON (MD '35)
AUGUST 20, 2000

JAMES CORRIGAN: AN ALL-STAR CAREER

BY ROBERT MENDELSON

Corrigan (with wife, Carolyn Corrigan) just stepped down as dean at Tulane.

COURTESY CORRIGAN

Dreams to become dean of a medical school aren't popular among youngsters. Certainly, in the 1940s and '50s, boys who grew up in Crafton, Pennsylvania, were more interested in one day playing baseball for the Pittsburgh Pirates.

"I was very definitely a Pirates fan," says James Corrigan, MD '61. But he was a fan of his dad, too. And when he realized he wouldn't be the Pirates' next second baseman, he thought he would become a dentist like his father (who graduated from Pitt's dental school). So at Juniata College, in Pennsylvania, he undertook a pre-dental/pre-medical curriculum. By his junior year, he had decided to become a physician. "Dad was disappointed," he says, "but very supportive at the same time." It wasn't as if he had dropped out of school.

During medical school at Pitt, Corrigan enjoyed working with children, especially at Children's Hospital of Pittsburgh—with one historic exception. It was in the pre-air-conditioning times of 1960, a warm and muggy autumn day. In an attempt to let in some air, most of the hospital windows were open. "I had a hard time concentrating," he remembers. Not because of the heat, though. A few blocks away, the World Series was taking place at Forbes Field. It was game seven and, for Pittsburgh fans, thank goodness neither Corrigan nor anyone other than Bill Mazeroski was playing second base for the Pirates. While Corrigan was checking on a patient, he heard a tremendous roar that stopped everything. Mazeroski had clubbed a home run to beat the New York Yankees.

The celebration was on. "After my shift, there was no way to get home. Huge crowds were mingling around on the streets. Traffic couldn't move, and all the streetcars were stopped. It was complete chaos."

Corrigan would go on to hit his own home run—in the field of medicine. He became a highly honored professor of pediatrics and internal medicine and, eventually, the dean of Tulane University's School of Medicine. He is the recipient of many honors, including the Ross Award in Pediatric Research (1975) and Pitt's Philip S. Hench Award (1997).

When he realized he wouldn't be the Pirates' next second baseman, he thought he would become a dentist like his dad.

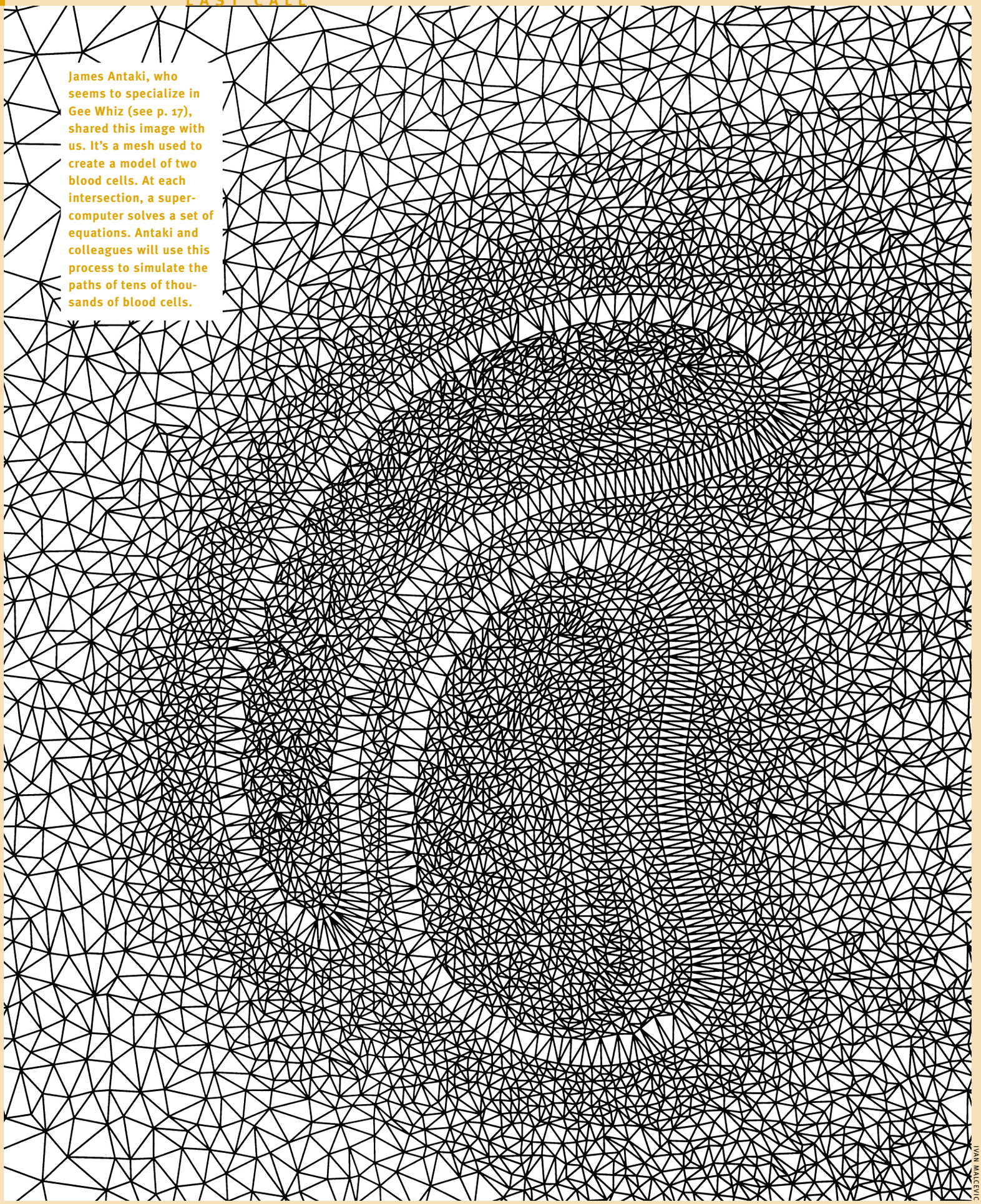
During Corrigan's tenure as dean, he oversaw significant growth of the school and modernized the curriculum.

"When I arrived here [as vice dean] in 1990, there wasn't one computer in the building for students." He is proud of Tulane's reputation and his legacy there. "The university is in the black, too, which is not always the case anymore, especially for private schools. One area that I do feel we need improvement in is research. We're not anywhere near Pitt, for instance, in regard to research dollars."

He stepped down from the deanship this July and will serve as vice president of Tulane's medical center. He's not looking back: "I was tired. I was well into my seventh year. Actually, I think unless you are a very unusual person, a dean ought to take on a job for five years. If you haven't completed your goals by that time, you're probably not going to do so."

Corrigan, 65, who continues to make rounds and teach, says he won't be retiring for some time. "When I make one more move—it's not if, it's when—it's going to be back west." Before his arrival at Tulane, he was at the University of Arizona for 20 years, where he served as chief of pediatric hematology/oncology and rheumatology and a professor. "We loved it out there," he says.

There will be another pilgrimage—east, however. "My 40th reunion is coming up. I'll be back." Maybe then, he'll glance at Forbes Field's left-field wall, which still stands on Pitt's campus, and think back to muggy autumn days at Children's Hospital. ■



James Antaki, who seems to specialize in Gee Whiz (see p. 17), shared this image with us. It's a mesh used to create a model of two blood cells. At each intersection, a supercomputer solves a set of equations. Antaki and colleagues will use this process to simulate the paths of tens of thousands of blood cells.

IVAN MALCEVIC

C A L E N D A R

JANUARY 20
FLORIDA ALUMNI RECEPTION
AND LECTURE
Longboat Key, Florida
For information
Jennifer Rellis
412-383-7619
jrellis@medschool.pitt.edu

MARCH 3
BAHNSON LECTURE
Irving Kron, MD, Speaker
Lecture Room 6
Scaife Hall, 10 a.m.
For information
Kathleen Haupt
412-648-9138
http://www.surgery.upmc.edu

MARCH 22
MATCH DAY
Lecture Room 4
Scaife Hall, noon
For information
Student Affairs Office
412-648-9040
student_affairs@medschool.pitt.edu

APRIL
SECOND ANNUAL PITT MED
GOLF OUTING
Date TBA
For information
golfouting@pittmed.pitt.edu

APRIL 21
14th ANNUAL
BLACK BAG BALL
Riverwatch
For information
Ross Musgrave, MD '43
412-648-9090
medalum@medschool.pitt.edu

APRIL 28
STARZL LECTURE
Rolf Zinkernagel, MD, Speaker
Lecture Room 6
Scaife Hall, 10 a.m.
For information
Kathleen Haupt
412-648-9138
http://www.surgery.upmc.edu

MAY 18
SENIOR CLASS LUNCHEON
The Twentieth Century Club
and
ANNUAL ALUMNI DINNER DANCE
Pittsburgh Athletic Association
For information
Ross Musgrave, MD '43
412-648-9090
medalum@medschool.pitt.edu

MAY 18 AND 19
CLASS OF '51 REUNION
Pittsburgh, Pennsylvania
For information
Robert Warner, MD '51
412-833-2032

MAY 18 AND 19
CLASS OF '61 REUNION
Pittsburgh, Pennsylvania
For information
Richard Paul, MD '61
412-683-1719

MAY 18 AND 19
CLASS OF '91 REUNION
Pittsburgh, Pennsylvania
For information
Andy Miller, MD '91
508-650-9181
andymiller66@hotmail.com

MAY 18 AND 19
SCOPE AND SCALPEL PRODUCTION
(More information to come)

MAY 19
DEAN'S BREAKFAST MEETING
Scaife Hall
For information
Ross Musgrave, MD '43
412-648-9090
medalum@medschool.pitt.edu

MAY 21
GRADUATION CEREMONY
Carnegie Music Hall, 10 a.m.
For information
Student Affairs Office
412-648-9040
student_affairs@medschool.pitt.edu

TO FIND OUT WHAT ELSE IS HAPPENING AT THE MEDICAL SCHOOL... http://www.health.pitt.edu

MERVIN STEWART, MD '53

LET'S DANCE

Are you ready to partake in fine food and spirits? Dance the night away? Rekindle vintage memories and friendships? Don't miss the University of Pittsburgh School of Medicine's Annual Alumni Dinner Dance on May 18. The gala will be held at the Pittsburgh Athletic Association and on hand will be this year's Hench Award winner, various University dignitaries, and many old friends. **Call the Medical Alumni Association for details: 412-648-9090**

Cheers!

UNIVERSITY OF PITTSBURGH
SCHOOL OF MEDICINE
M-240 SCAIFE HALL
PITTSBURGH, PA 15261

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