

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE | FEBRUARY 2004

# PITTMED

LESSONS FROM  
A DARK WINTER

THINK THE UNTHINKABLE







## FIRST FAMILY OF MEDICINE

Dr. Jessica Lewis was a special person, and I am honored to say that I knew her, worked with her, and did work for her—she will be missed greatly.

Deborah S. Small  
Pittsburgh

I thoroughly enjoyed Edwin Kiester's article on Dr. Jack Myers. I graduated from Pitt med in 1975 and did a senior elective in computer medicine with Dr. Myers, Randy Miller, and Harry Pople. Randy was a fellow student; he convinced me to take the elective. I was rather intimidated at the thought of working one-on-one with Dr. Myers, but it turned out to be the highlight of my med school years. Dr. Myers must have mellowed some; as long as I was prepared with my presentations, he was fair and always encouraged us to "research our topics more." His letter of recommendation was influential in helping me obtain my residency.

The article was accurate and truly captured the aura of his teaching and research. His memory and diagnostic abilities were intimidating to everyone. The diagnostic computer program that he developed, which eventually became QMR, basically put his vast medical knowledge and clinical experience into a database. His clinical diagnostic skills will probably never be duplicated.

I also had the opportunity to witness his expertise in classical music.

I am currently working in the ambulatory care clinic at the James Haley VA in Tampa, after having tossed in the towel from private practice after 16 years and a five-year trial at a staff model HMO. Pitt med prepared me incredibly well for my residency. Dr. Myers preached about paying attention to details, being prompt, and being humble—traits I always attempt to maintain. Unfortunately, with the high volume of demands on primary care physicians and the dumbing down of medicine by HMOs, I'm afraid these goals are almost impossible to attain, except at great personal expense.

I look forward to reading future articles by Mr. Kiester.

Douglas A. Saslow (MD '75)  
Tampa, Fla.

It has been more than 40 years since I completed my internal medicine residency under the tutelage and teaching of Dr. Jack Myers, one of the finest bedside diagnosticians of the last century. Hungry to learn more, I repeated my first-year residency just so I could spend more time with the ward service and Dr. Myers. I looked forward to the "Morning Reports" and the medical rounds.

Jack Myers was a teacher and superb medical role model in an era when history-taking and

physical diagnosis were extremely important. As a diagnostician, Myers had few equals, if any.

He was a friend to every medical house officer and could always be approached for advice on problems outside of medicine. I know from personal experience his caring qualities.

He inspired an entire generation of men and women to become better, caring physicians. Even now, in my medical practice, when faced with a tough medical diagnosis or decision, I often ask myself, *What would Jack do?*

Stanley P. Silverblatt (MD '57, Res '61)  
Hallandale, Fla.

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

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# PITTMED

UNIVERSITY OF PITTSBURGH SCHOOL OF MEDICINE MAGAZINE | FEBRUARY 2004, VOL. 6, ISSUE 1

## DEPARTMENTS



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No one had seen ambulance attendants like these before.

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Identifying the 20,000 human remains from the World Trade Center. Public health is never dull when Bruce Dixon is involved.

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This will hurt us more than it hurts you.



## CONTRIBUTORS

**MEGHAN HOLOHAN** ["Lean on Me"], *Pitt Med*'s assistant contributing editor, will follow a story almost anywhere. Most recently she has been reporting on doctors working in homeless camps and clinics in Pittsburgh and Boston; she's on the street even when the mercury dips below freezing. We figured she had the constitution to deliver on her next assignment: the making of this year's Scope and Scalpel, which she says promises to be as satirical and tacky as its predecessors.

After some 15 years of creating professional illustrations for clients that include *The Atlantic Monthly* and *The New York Times*, **DAVID POHL** [cover, "Lessons from a Dark Winter"] had a mid-life artistic crisis. For several months last fall, he stopped taking commercial assignments so he could focus on reinventing his work. This issue's cover is the first time that he's used his new illustrative style for a commissioned piece.

## COVER

About the cover: If you're going to be ready for a bioweapons attack, the first thing to do is imagine it actually happening. (© David Pohl.)



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The best, and perhaps most instructive, day of the week for these students is when they stop in to visit patients they've befriended.

BY MEGHAN HOLOHAN

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Finding more effective treatments for arthritis is going to take researchers with persistence. It's a good thing Constance Chu is committed to the task.

BY DOTTIE HORN

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Pittsburgh is now the headquarters and proving ground for academia's top biosecurity think tank.

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BY ROBIN MEJIA

# PITTMED

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A Zuni myth tells the story of Kiaklo, who, when sent by his people to scout northern lands, became lost in the hidden world beneath the snow. Cold, lame, and blinded by the white landscape, Kiaklo's very heart died; he cried continuously until he came upon a duck, whose cry was like his own, and he sought out her counsel. She assured him she knew of his country, so he followed her home on a worm that had transformed itself into a rainbow.

We may be worlds away from the mythological realm of the Zuni people, who reserved an honored place in their culture for animals, yet animals still have the power to, in a sense, point us to where we came from. Charles Darwin was one of the first naturalists to appreciate the notion of an animal model for the study of the human condition. In 1872, he wrote a book that remains fresh for those with an interest in comparing emotional expression between animals and humans to illuminate core themes in human behavior—themes that have been conserved through evolution and not been confounded by social structure and culture. Here is Darwin on cats, when terrified: *[they] stand at full height, and arch their backs in a well-known and ridiculous fashion .... the hair ... becomes erect. ... I am inclined to believe that, in the same manner as many birds, whilst they ruffle their feathers, spread out their wings and tail, to make themselves look as big as possible, so cats stand upright ... arch their backs ... and erect their hair.* Does this not bring to mind colleagues who, anxious about their standing among their peers, “puff themselves up”?

The advances made by scientists driven to learn what other beings can tell us sound like the makings of modern myths: Imagine—fish may help repair a heart condition in infants. The zebra fish has the facile genetics of a fruit fly, but, like us, it is a vertebrate and shares many of our key genes. A particular zebra fish mutant has been found with diminished blood flow through its aorta. Researchers have identified a similar, if not identical, mutation that gives rise in human infants to coarctation of the aorta. One can imagine a gene-based screening to ensure recognition of the need for surgery at the earliest possible time. Even more fantastic—might a worm reveal secrets of long life? *Caenorhabditis elegans*, the worm which was the subject of last year's Nobel Prize, may be our best model for understanding aging. Amazingly, worms with a mutant *daf-2* gene live twice as long as normal worms. The mutation allows them to outlive unfavorable environments (e.g., no food) and postpone reproduction in such environments. These phenomena seem to involve the insulin pathway. Again, a seemingly simple organism will teach us much about human biology and disease.

In this issue, we describe the establishment of our facility for zebra fish research. In fact, we are investing much thought, effort, and monies in quickly developing one of the nation's leading such facilities, with plans for 10,000 fish tanks and a half-dozen principal researchers (“zebrafishermen”) in Biomedical Science Tower 3, the extraordinary research building we're now constructing. Next in line for a major new effort in developmental biology here will be that wiggly Nobel laureate, *Caenorhabditis elegans*. As the worm turns, so will we!



JULIA MAROUS STRAUT

Arthur S. Levine, MD

Senior Vice Chancellor for the Health Sciences

Dean, School of Medicine



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## Lauterbur Gets Nobel

In the early 1980s, when magnetic resonance imaging equipment first was used clinically, Paul Lauterbur attended a meeting of radiologists to explain applications of MRI technology.

After giving his presentation, Lauterbur overheard an older radiologist grumble, "I am glad that I am old enough to be retiring. Now I don't have to learn all this stuff."

"This stuff" changed the field of radiology, allowing doctors to have images of internal organs, tissues, and tumors. Today, approximately 22,000 MRI scanners are in operation worldwide, and about 60 million scans are performed a year.

Lauterbur, who received his PhD in chemistry from the University of Pittsburgh in 1962, remembers thinking there had to be a better way than exploratory surgery for doctors to examine tumors and organs. He was familiar with imaging techniques. In the '50s and early '60s while working at the Mellon Institute, Lauterbur studied the carbon-13 isotope with nuclear magnetic resonance (NMR), a technology mostly used by chemists to determine the structure of molecules by subjecting atomic nuclei to a magnetic field. Lauterbur was eating a hamburger at a Big Boy in New Kensington when he realized that NMR could identify the location of hydrogen nuclei to produce images of the body. It took years of experimentation before Lauterbur was able to develop the clinical technology that became known as MRI.

Last fall, the Nobel Assembly recognized Lauterbur's achievements, awarding him and Sir Peter Mansfield the Nobel Prize in Physiology or Medicine. The committee praised Lauterbur for adding gradients to a magnetic field, recording its emitted radio waves, and creating two-dimensional images of objects (his first images were of two tubes of water). The committee recognized Mansfield for improving the use of gradients, which produced a sharper image.

Lauterbur still applies imaging in his research at the University of Illinois in Urbana. He now uses NMR to try to determine how proteins contributed to the beginning of life on Earth. —*Meghan Holohan*

Paul Lauterbur (left) receives his prize from the king of Sweden



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## FLASHBACK

Astronomer Percival Lowell insisted until his death in 1916 that his observations of Venus revealed dark spokes radiating from a hub on the planet's surface. Only last year, doctors realized that when Lowell narrowed the aperture of his 24-inch telescope down to three inches or less (to reduce the planet's brightness), he had created the world's largest ophthalmoscope, which cast the shadows of blood vessels in his own retina onto the image of Venus.





A&Q

## Shanthi Trettin, on Fashion and Medicine

"I'm curious about a lot more than the physical body," says Shanthi Trettin (Class of '04). After five years at Pitt, Trettin (shown above) will graduate this spring with an MD and an MA in bioethics, as well as two area of concentration program certificates—in medical humanities and women's health. Her plans include clinical psychiatry, humanities research, and teaching in an interdisciplinary setting. A former immunology researcher, Trettin is one of only a handful of Pitt med students to complete a bioethics degree.

### On why she studied fashion images as part of the research for her thesis

In thinking about those things that make patient care less effective and less compassionate than it could be, my question was: What's wrong with our whole culture? How is the separation between the mind and the body perpetuated, and what processes are involved in such dualism? That's why I look at fashion—which is an extreme of people being treated as objects, being fragmented, and being homogenized.

### On her analysis of images of models in *Vogue* magazine

A lot of times faces are masked in these emotionless expressions, so there's a mind-body disconnect. That's an example of how the images are objects. ... Sometimes the whole body is shown, but the shirt shows a little fragment of nipple, so the viewer's gaze is directed at that little fragment of the person. The body is framed in a way that the viewer's attention is on a fragment. ... Homogenization is more obvious—every single model is tall and skinny.

### On how Western dualism manifests itself in medicine

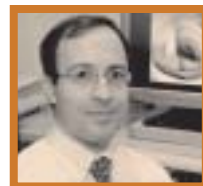
The biomedical model is reductionistic—it breaks individuals down into smaller and smaller categories; for example, you have your eye doctor, your heart doctor. So on one level, you're broken up into organs. People end up being defined by their problem or by their body part. ... [Patients are homogenized] within their disease group and their population. So, assumptions are made based on someone being lesbian or heterosexual. Not all those things are bad—some are necessary in order to diagnose and treat disease. [What is lost in the biomedical model is] the inherent connection between different aspects of a person's life. [A person's] financial situation, religious beliefs, and broken knee may all be totally intertwined.

### Her question for the world

As physicians, [how] can we better interact with our patients in a way that acknowledges the mind is connected with the body and the individual is necessarily embedded in his or her cultural context, including family environment, religious beliefs, economic situation, and social aspects? —Interview by Dottie Horn

## Faculty Snapshots

**M**ore frequent screening for colon cancer could save lives, suggests a study by **Robert Schoen**, professor of medicine. The MD's study was published July 2 in the *Journal of the American Medical Association*. Schoen studied flexible sigmoidoscopy, a screening test used to examine the lower half of the colon; current guidelines recommend that the test be repeated every five years. Schoen studied more than 9,000 people who came back for a repeat flexible sigmoidoscopy after three years. A little more than 3 percent of the study participants had developed a nonadvanced adenoma (growth), while 0.8 percent had an advanced adenoma or cancer. His study raises questions not only about the frequency of screening with sigmoidoscopy but also about the 10-year interval that is currently recommended between colonoscopies, which examine the entire colon. Doctors may miss more cancer by examining the entire colon every 10 years than by examining half the colon every five years, he says.



Schoen

A bone marrow transplant can cure sickle cell disease—but it has risks. Five percent of sickle cell transplant patients have died, largely because they become severely vulnerable to infection when chemotherapy destroys their native marrow. **Lakshmanan Krishnamurti**, assistant professor of pediatrics, and **Andrew Yeager**, professor of medicine and pediatrics, hope to develop a safer way to transplant bone marrow in sickle cell patients. They have begun a research study and plan to enroll 20 patients throughout the next five years. Participants will receive less than half the usual amount of chemotherapy prior to transplant. Their native bone marrow will not be wiped out entirely, so after the transplant, the doctors will administer higher doses of immunosuppressive drugs—which they hope will allow the native and donor marrow to reach a state of mutual tolerance. The doctors recently used their regimen while performing Pitt's first bone marrow transplant given in an attempt to cure sickle cell disease. Their patient, a 5-year-old boy, is doing well so far.

For years, doctors have reported that when patients are infected with HIV, their cholesterol levels drop. But when HIV-infected patients receive highly active antiretroviral therapy (HAART), their cholesterol levels rise. A new study by **Sharon Riddler**, assistant professor of medicine and an MD, shows that, after treatment with HAART, cholesterol levels return to about what they were prior to HIV infection. The rise after the initiation of HAART probably reflects the body's return to a healthier state. Her paper was published June 11 in the *Journal of the American Medical Association*. —DH



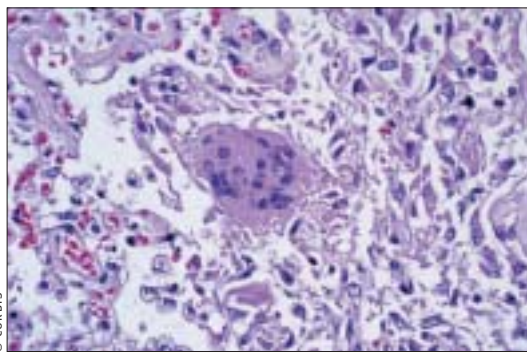
Riddler

# Racing Against SARS

Even by modern standards, the speed with which the scientific community has attacked SARS (severe acute respiratory syndrome) is remarkable. Consider what occurred over two months last year. In February, the World Health Organization noted a few hundred cases of severe atypical pneumonia; the outbreak hit China, Vietnam, Singapore, and Canada. On March 17, the WHO mobilized a global network of laboratories to work collaboratively on the new disease. On March 24, scientists in Atlanta and Hong Kong isolated a new coronavirus from patients with SARS. On April 12, Canadian researchers announced they had successfully sequenced its genome.

At Pitt, the search for a vaccine began soon after, and it has yielded some tantalizing early results. In June, a Pitt professor of surgery and medicine, Andrea Gambotto of the Molecular Medicine Institute, along with others from the School of Medicine and the Graduate School of Public Health, produced an experimental vaccine by genetically engineering a common-cold virus to express three SARS genes. In July, they injected a group of rhesus macaques with the virus. Six weeks later, T-cells and antibodies against SARS were discovered in all of the immunized monkeys and none of the control group. Their results were published in a fast-track letter in *The Lancet* on December 6.

It's uncertain if this will lead to a vaccine for humans. Macaques don't present SARS symptoms, so the next step is to test the vaccine in animals that do get SARS. One possible pitfall: Some experimental vaccines actually enhance disease symptoms instead of preventing them. Gambotto's group needs to determine whether this is the case before even considering testing the vaccine in humans. —Chuck Staresinic



The SARS virus. Gambotto has developed an experimental vaccine.

## THE ROAD LESS TRAVELED

**Ann Willman (Class of '08) sat in a clinic, talking with an ovarian cancer patient. "The experimental drug targets receptors on the cancer cells," she explained. As a clinical research coordinator at Dana-Farber Cancer Institute in Boston, Willman loved helping patients understand diseases and treatments. And patients seemed to appreciate becoming better informed and taking part in research. Those interactions eventually drew Willman to pursue a career in clinical, rather than basic, science research.**

**Willman is one of the first medical students to participate in the School of Medicine's new Clinical Scientist Training Program. She will study not only medicine but also biostatistics, clinical trial design, and research ethics. She'll work with a senior faculty member to develop her own research projects. With mentoring and support, Willman is expected to publish in peer-reviewed journals and present at national conferences. In five years, she'll graduate with an MD and MS in clinical research, as well as a head start on a road less traveled. Pitt started the Clinical Scientist Training Program partly because of the alarming national decline in the number of clinical researchers.**

—Corinne Bechtel



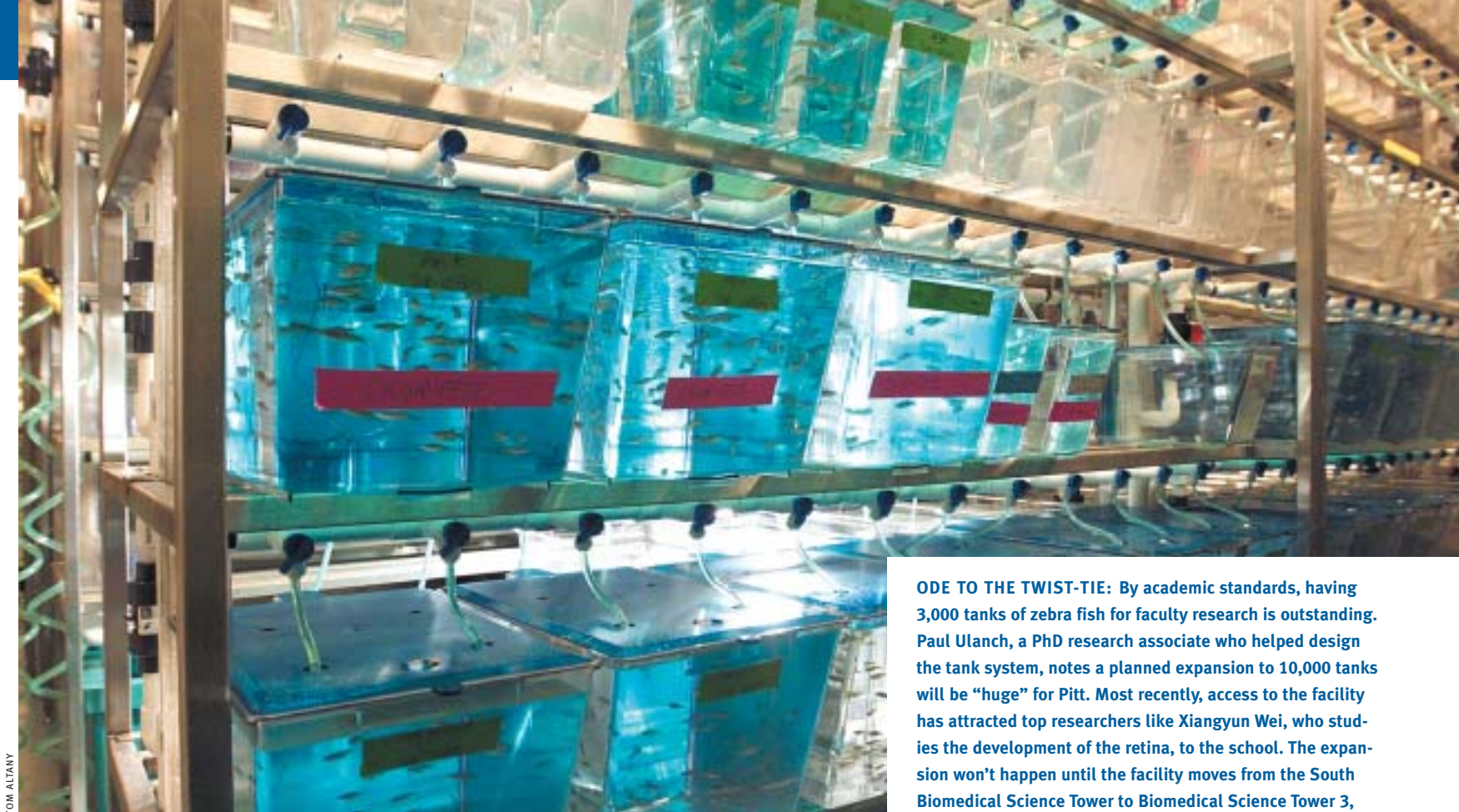
Vanesa Rawe

## Americas Fellow Looks at Infertility

As a scientist working in her native Argentina, Vanesa Rawe would order antibodies needed for experiments from U.S. companies. It would take two to three weeks for the antibodies to arrive, and they would cost double the catalog price owing to shipping charges and import taxes. As a postdoc at Pitt, Rawe can now get the antibodies in two days (plus she works with better equipment). In 2003, the National Institute of Child Health and Human Development awarded Rawe an Americas Fellowship—an honor given each year to a handful of Latin American PhDs doing reproductive research. The fellowship provides funding for up to two years of advanced training in the United States. Rawe is working in the lab of Gerald Schatten, professor and director of the Pittsburgh Development Center—where she attempts to better understand, at the cellular and molecular levels, normal fertilization and problems that lead to infertility.

"Her long-term, demonstrated commitment to basic-science inquiry of increasing complexity, as well as her technical prowess at assisted reproductive technologies and microscopy, won her this well-deserved award," says Schatten. Rawe plans to return to Argentina in 2005. —DH





TOM ALTANY

**ODE TO THE TWIST-TIE:** By academic standards, having 3,000 tanks of zebra fish for faculty research is outstanding. Paul Ulanich, a PhD research associate who helped design the tank system, notes a planned expansion to 10,000 tanks will be “huge” for Pitt. Most recently, access to the facility has attracted top researchers like Xiangyun Wei, who studies the development of the retina, to the school. The expansion won’t happen until the facility moves from the South Biomedical Science Tower to Biomedical Science Tower 3, which is now under construction. How will all those fish be moved? Ulanich isn’t 100 percent sure: “Baggies?”



Hillier

## Appointments

**Sharon Hillier** was recently elected president of the Infectious Diseases Society for Obstetricians and Gynecologists. She is the first woman and the first non-MD to head the organization, which is an arm of the American College of Obstetrics and Gynecology. Hillier is a PhD and a professor of obstetrics, gynecology, and reproductive sciences and of molecular genetics and biochemistry in the School of Medicine. She has found that a common

vaginal condition called bacterial vaginosis (BV) puts women at increased risk for getting genital herpes. BV, which is believed to affect one in seven women, is characterized by a change in the pH and bacterial population in the vagina; the disease can be asymptomatic or can result in a vaginal discharge or odor. Hillier hopes her findings will lead to more aggressive treatment for BV—currently, the disease is generally not treated if it is asymptomatic. “Even common vaginal conditions, like BV, that people have thought of more as a nuisance rather than a

real medical problem, may play a real role in enhancing the spread of herpes,” says Hillier, noting that the disease is becoming more widespread: “We’ve seen a doubling in genital herpes in the past decade, even though, supposedly, it’s the era of safe sex.”

## 65,000 SCIENTISTS STRONG

Not every scientist takes a stand on Capitol Hill—but Robert Wells does. Wells is director of the Center for Genome Research at Texas A&M University, Houston, and a 1964 PhD graduate of the School of Medicine. As president of the Federation of American Societies for Experimental Biology (FASEB), he urges Congress to increase funding for the National Institutes of Health, the National Science Foundation, and other federal agencies that support scientific research. Such lobbying is part of FASEB’s mission; the group is a consortium of 22 scientific societies, including the American Society for Clinical Investigation and the American Physiological Society, and represents 65,000 scientists. As FASEB president, Wells is involved in responding to inquiries from members of Congress and their staffs about a variety of scientific issues, including the use of stem cells and animals in research. One of Wells’ goals is to build ties between FASEB and the American Mathematical Society, the American Physical Society, and the American Chemical Society—alliances that will strengthen the lobby for increased funding. “Excellent progress in biomedical sciences depends on excellence in the underpinning sciences, such as mathematics, computer science, chemistry, even physics,” says Wells. —DH

A mouse’s heart beats 10 times faster than a human’s—650 times a minute. And mice are helping researchers understand human arrhythmias—irregularities in the rhythm of the heartbeat. **Barry London**, the new chief of the Division of Cardiology, uses mouse models to identify genes that control the electrical activity of the heart. He also studies human families with a rare form of inherited arrhythmia—he hopes to identify the genes responsible for their disease. His research could help doctors identify which patients with arrhythmia are most at risk for sudden death—and thus which patients are the best candidates for treatment with an implanted defibrillator. In his new role as division chief, London, an MD and PhD, plans to recruit more basic science faculty, particularly those who study blood vessels and what leads to their becoming blocked. —DH



London



## ONE STEP CLOSER

A NIGHT IN THE ER  
BY JOSIE FISHER

**B**efore the evening shift in the emergency department at UPMC Presbyterian, Jonathan Landry (Class of '06) hunts down the free soda machine in the EMT room. He inhales a cup of syrupy Pepsi before finding Susan Dunmire (MD '85), associate professor of emergency medicine. She briefs him on the patient triage chart—color-coded squares on a computer monitor: “The back 15 rooms are yellow, for critical, and trauma is red.”

Landry jumped at this opportunity, facilitated by the University of Pittsburgh's Emergency Medicine Student Association, to shadow a physician in the ED. The student thinks he wants to go into emergency medicine but hasn't ruled out other possibilities. “I need to see if this is what I want to do,” he says.

He follows Dunmire into the room of a patient with metabolic acidosis—the man's blood pH level is low. When they walk out of the exam room, Dunmire quizzes him: “Do you remember your MUDPILES?” MUDPILES is a mnemonic for factors that can cause one type of acidosis. Landry begins: “M for methanol, U for uremia ....”

“Very good,” says Dunmire, “Get his blood pressure and ask again about alcohol and meds.”

Landry returns to the patient's room. The patient twitches nervously as Landry applies a blood pressure cuff and questions him. Later, Landry reports his findings to Dunmire, noting that the patient seemed defensive in his vehement denials of any drinking. His symptoms—pain, difficulty eating, and a couple of unusual lab results—don't add up to anything concrete. Dunmire decides to send him for further testing and to admit him to the hospital.

For Landry, it is a lesson in the nature of emergency medicine. In the short time frame of the ED, doctors may not always get to the bottom of patients' conditions. There's not always a sense of closure.

Landry heads over to the trauma bay as a car accident victim arrives. He joins a bevy of



CAMI MESA

Jonathan Landry is one of many students who “try on” emergency medicine.

others looking on as the trauma team and ED staff treat the victim. It's frustrating not to be involved with the case, admits Landry. He wishes he was at a level of training that would enable him to help the team resuscitating the patient.

Despite the minor frustration, the night reinforces Landry's interest in emergency medicine. He likes the variety of cases he sees—a patient whose pacemaker is in overdrive, a man with dementia, a woman being evaluated for involuntary psychiatric commitment. He feels the intensity of the ED is more suited to his personality than a “drier” environment. He has shadowed before in non-ED settings, but those experiences didn't make him feel “as alive.”

Shadowing will help him make some decisions about his future. Even with clinical rotations, med students are not exposed to every single specialty and subspecialty. Shadowing enables students to fill in the gaps and experience areas of special interest. And Pitt is a great place for such exploration, notes Landry:

“Physicians who come in to do PBLs [problem-based learning sessions] love to invite us to go on rounds with them.” The opportunities to shadow physicians are, Landry says, “limitless.” ■

*Some details in this story have been changed to protect patient privacy.*

## PRACTICE, PRACTICE, PRACTICE

More than a dozen medical students gather around tables piled with catheters, tourniquets, and tubing at this workshop sponsored by the Emergency Medicine Student Association (EMSA). A nurse demonstrates how to insert an IV. As blood appears, several students look away or cover their mouths; one sheepishly admits she feels woozy. The nurse removes the needle with ease. They have questions: “When you pulled that out, how did you make sure blood didn't spray everywhere?”

“It's a vein. It wouldn't do that,” she replies.

Second-year medical student Adam Tobias seems nervous as he looks over his classmate's arm, preparing him for the procedure. “Look how hairy your arm is,” he exclaims, rolling up the sleeve. Tobias applies the tourniquet over the sleeve. (The nurse has told the group this avoids causing pain to hairy arms.)

Tobias is a cocordinator of EMSA. Through the group, he has seen x rays of fractures and bullet wounds and learned about common overdoses. He has heard a case history of a meningitis patient and has practiced drawing blood and suturing pig's feet. The workshops give him practical advice and opportunities he's not likely to get from a textbook or lecture. Another advantage: As you give up your arm to your classmate's needle, he says, you experience the patient's point of view. A moment of reckoning.

Tobias hesitantly taps the inside of his classmate's arm, looking for a vein. —CB

## INVESTIGATIONS

*Explorations and revelations taking place at the medical school*



This humanoid is failing fast.



# A GROWING SIM FAMILY

PAY NO MIND TO THE PROFESSOR BEHIND  
THE CURTAIN | BY RONAL MITCHELL

**O**n the videotape is a Pitt med student (we'll call him Eric Marks) wearing indigo scrubs. He stands near a mannequin on a gurney. It's his first day in a four-week critical care medicine course. The life-size humanoid on the bed is SimMan, a computerized patient simulator. SimMan audibly breathes, his chest moves up and down, and he has a pulse, heart rhythms, and blood oxygen levels, among other features. Today, the mannequin is undergoing cardiac arrest—and Marks is called upon to lead a group of students responding to the crisis.

It's an urgent situation for SimMan, but instead of checking his vital signs, Marks stands motionless, asking the mannequin a series of questions: "Do you have a history of injuries to the chest? Can you climb a flight of stairs?" His bedside manner is terrific, yet SimMan, whose pulse is getting weaker and weaker, can barely summon the breath to reply. A person behind a curtain, much like the Wizard of Oz, speaks for SimMan; the voice is broadcast into the room where SimMan lies. Nine minutes into the exercise, Marks finally puts a blood pressure cuff on the mannequin and monitors the heart rate. Other students apply an oxygen mask—but they do it incorrectly, and it doesn't work. The steady blip of the heartbeat becomes irregular. The students try to insert a breathing tube but fail. The heart monitor displays an eerie flat line as it lets out a high-pitched beep.

Nervous chatter ensues throughout the room as Marks looks blankly at the equipment and his patient, wondering where he failed.

The hands-on exercise for Marks and his classmates is the stuff of a typical day at Pitt's Peter M. Winter Institute for Simulation Education and Research (WISER)—the largest civilian simulation center in the world. In 2002, WISER hosted 7,000 educational simulation experiences. Using SimMan, trainees can practice key skills—such as responding to a drug overdose, administering anesthesia, inserting a bronchoscope into a

lung, or putting a central line into a neck vein without puncturing an artery or damaging the vocal cords. The center has 12 rooms set up for teaching, is home to 14 mannequins, and provides training to med students, residents, and fellows—it even offers refreshers so that faculty can brush up on skills.

Some of the mannequins are specialized. One, with splotches of fake red blood on his plastic body, has a broken foot, a snapped bone protruding from his leg, abdominal injuries, and a piece of barbed wire piercing his face—plus, he's in cardiac arrest. (His story: He suffered a myocardial infarction while mowing the lawn, fell down a hill, onto a fence, and the mower fell on top of him.) This memorable mannequin teaches students how to establish priorities: When someone comes into the emergency department with multiple traumatic injuries, how do you decide what to do first?

Although the mannequins can be used to mimic many different medical situations, the underlying goal of simulation education is always the same: Give trainees hands-on practice without posing any risk to patients. In most medical schools in the country, students learn clinical skills primarily through observation and by performing procedures on real patients under supervision, notes Tom Dongilli, WISER's director of operations. Pitt's facility gives students the opportunity to practice procedures first—and to get lots of practice. Before graduation, every Pitt med student spends 50 hours learning in WISER. The majority of students elect to take the fourth-year critical care medicine rotation, as Marks did—which means they spend an additional 40 hours learning in the facility.

The intensity of simulation education at Pitt is so unusual that every year about 4,000 visitors—many from other medical schools—tour the facility. (And that's not counting the 3,000 prospective med students who visit the center annually.)

Simulation research is also part of WISER's mission. In 1996 (before WISER

was created), John Schaefer, now director of the institute, and René Gonzales, a former Pitt anesthesiologist, created and patented the simulator AirMan. Their invention was an improvement on previous simulators, and Laerdal Corporation, in Norway, licensed the patent, manufactured AirMan, then later upgraded AirMan into a yet more sophisticated model, the present-day state-of-the-art SimMan.

The Sim family is growing. In one of the rooms at WISER, a simulator prototype sits on a patient examination table; a small plastic chest is dismantled, with mechanical parts strewn about. It's SimBaby—a Laerdal creation. The pint-size mannequin will help medical trainees confront the challenges posed by an infant's physiology. For example, to insert a breathing tube into an infant, the neck and body must be positioned in a different way than when inserting a tube into an adult.

When SimBaby becomes available for sale later this year, it will have grand mal seizures, its lips and fingernails will turn blue to indicate lack of oxygen, and its pupils will dilate and contract. No other simulator can get sick in those ways. Every few weeks, Laerdal sends a new version of SimBaby to WISER for testing—the institute is helping to develop the mannequin into a more useful and sophisticated tool.

Four weeks after Marks' debut in critical care medicine, the med student tries again. He has received feedback from his instructor on his initial performance. His videotaped session with the mannequin (there are tiny cameras in each simulation suite) was accessible through the Internet for Marks to review. Now, he is back in action. SimMan is suffering, yet again, from cardiac arrest. This time, Marks takes charge of his team of students immediately. He has them get an IV going and an oxygen mask placed; he checks the pulse. When the heart stops, he tells his classmates to start CPR. He directs the use of a defibrillator. SimMan's heartbeat comes back, steady and strong. ■

# KINDRED SPIRITS

CLOISTER FELLOWS DELVE INTO LIFE AT NIH | BY LOIS BARON

The communal dinners take place twice a week. It's dark outside by the time you sit down to eat the surprisingly good food off the buffet line. It feels cozy because you're with kindred spirits. The people here are as interested in science as you are. On Monday night, the speaker might be the man who invented the celebrated cancer drug Gleevec. On Thursday nights, it's two fellow students who are also doing

And they're digging in to sample it all.

For the 2003-'04 academic year, 179 medical and dental students from around the country applied, and 42 won fellowships. (In addition to a stipend and subsidized housing, they also get a parking place—a privilege normally reserved for VIPs like institute directors.)

The HHMI-NIH scholars choose the lab in which they'll work. Options include those

The lab Shen works in is examining a hypothesis generated from the findings of Steve Rosenberg, an NIH researcher. Rosenberg successfully treated metastatic melanoma by taking a biopsy of a tumor, extracting immune cells (lymphocytes) embedded in the tissue, growing the cells in culture, and injecting large numbers of the cells back into the patient to proliferate and resist the cancer.

It stands to reason that the treatment might work better if it used immune cells that can divide many, many times—indicated by longer telomeres. So the lab explores whether patients who respond well to Rosenberg's therapy have immune cells that differ in telomere length from patients who don't.

It was important to Muhly to have a lot of interaction with his primary investigator, so he chose to work with Michael Iadarola. Not only did Muhly opt for an energetic PI who is around a lot, but also, with Iadarola, he found a research topic of great clinical import. The lab, part of the National Institute for Dental and Craniofacial Research, explores how neurons respond to painful stimuli. Muhly and his new colleagues want to learn which genes are turned on when animals are exposed to irritants. "If we can figure out how neurons respond to noxious stimuli, we might be able to design drugs that block the painful signal carried by the neuron before it reaches the brain," Muhly says. And doctors will likely treat more chronic pain as life spans extend, and the baby boomers march into advanced ages.

Like most of the HHMI-NIH fellows, Muhly (with his wife) and Shen live in the Cloisters, an old monastery tucked into a corner of the NIH campus. The shared living facility contributes to the communal atmosphere.

"Everyone here is very involved in science," Shen says. He never gets a blank look when he describes his work. "It's easy to talk with people who understand what I'm saying."

And at those biweekly dinners, Shen, 24, is astounded at how ably the fellows discuss NIH research. "We're so young, but we sound like real scientists," he says. ■

Ty Muhly (left) and Xinglei Shen



STEVE HOOTON/PICTOGRAM STUDIO

research at the National Institutes of Health (NIH). You learn about tumor immunology, multiple sclerosis, how brain structure changes with addiction.

Wallis "Ty" Muhly and Xinglei Shen (both in the Class of '05) came to the red-brick, lush-green-grass NIH campus in Bethesda, Md., last summer as fellows in the one-year Howard Hughes Medical Institute–National Institutes of Health (HHMI-NIH) Research Scholars Program.

of more than 1,200 NIH researchers working on more than 2,500 research projects.

For Shen, the deciding factor was the chance to study the telomere—a cell structure that piqued his interest in high school. Telomeres are repeating sequences of DNA that appear at the ends of chromosomes. Because these sequences get shorter each time a cell divides, telomere length signals how close a cell is to senescence and no longer replicating.



# WHAT STOKES A BELLY OF FIRE

CELLS LINING BLADDER  
SIMILAR TO NERVES  
BY KRISTIN OHLSON

**S**ome patients describe it as a belly full of broken glass, some as a fire deep in the abdomen. The 700,000 people in the United States who have interstitial cystitis feel pain and intense urgency to urinate even with only tiny amounts of urine in their bladders. They have to run to the bathroom frequently—up to 60 times a day in the worst cases, even at night. Under the stress of all this discomfort—and with no cure in sight—some patients become suicidal.

No one knows why people get interstitial cystitis, a chronic inflammation of the bladder. It has no identifiable bacterial cause. A few treatments can provide temporary relief, but no one knows how to cure the disease; it doesn't respond to antibiotics or other drugs that cure urinary tract infections.

Those studying the bladder typically hadn't given much thought to the urothelial cells as a source of the pain of interstitial cystitis. These large cells line the inside of the bladder and stretch and contract depending on how much urine is inside. They fit together so tightly that they protect the underlying layer of nerves and other more delicate tissues from toxic substances in the urine.

"People used to think of the urothelium as simply a barrier that protects the underlying tissue," says Lori Birder, assistant professor of medicine in the University of Pittsburgh School of Medicine. "People thought of it as a passive tissue that didn't have anything to do with sensation."

Birder changed this perception a few years ago when she discovered that these urothelial

cells have some sensing behaviors that are similar to those of neurons. She had been conducting studies with capsaicin, the chemical that makes chili peppers hot. Capsaicin is used clinically for temporary pain control—it can desensitize nerves that carry pain signals. Some people with interstitial cystitis are treated by having their bladders filled with a solution containing capsaicin, which relieves some of their symptoms for a while. Birder studied the effect of capsaicin on strips of tissue from human bladders containing all the component parts—urothelial cells, nerves, and muscles. She assumed that only the nerves underlying the urothelium would be affected; she was wrong. The urothelial cells reacted to the chemical. In this and subsequent studies, Birder—who received a Young Investigators Award from the International Union of Pharmacology for this work—showed that the urothelial cell receptors released substances that a neuron would, like nitric oxide. As it turns out, the cells release transmitters and other mediators. And these actions can trigger an increase in neural activity, intensifying pain.

Her discovery suggests that, through

messengers such as the transmitters and mediators, urothelial cells "talk" to the underlying nerves. "If there's an inflammation, the urothelial cells might 'talk' more, so that the person feels pain even if there is only a normal amount of urine in the bladder," says Birder. She suspects this happens when the bladder is inflamed or injured.

Eventually, Birder's work may give drug companies more options for the development of pain medications for people with interstitial cystitis. Drug companies are already working on compounds that target the bladder nerves, but it's possible that they may find different substances that target the urothelial receptors.

"In the last few years, a lot of new surprises have emerged regarding the role of these cells in bladder function," she says.

Birder continues to explore the nervelike properties of urothelial cells and to study the role the cells may play in interstitial cystitis. One finding: Cats with naturally occurring forms of interstitial cystitis have abnormalities in their urotheliums. Birder believes the urothelial cells may also be implicated in other conditions that can affect bladder function, such as diabetes and spinal cord injury. ■

Lori Birder was the first to show that urothelial cells (stained green) contain TRPV1 receptors (stained red). Previously, scientists thought that the TRPV1 receptors were found only on nerves. Her finding suggests that urothelial cells may contribute to pain in conditions such as interstitial cystitis.

COURTESY L. BIRDER





In his classes, Rich  
Julyan would hear that  
where people live  
affects how they care  
for themselves.  
However, he couldn't  
grasp how until he went  
into a patient's home.



THE BEST DAY OF THE WEEK

BY MEGHAN HOLOHAN

# LEAN ON ME

**R**ich Julyan walked up steep stairs that bowed in the middle, making his way to the door on the third floor. He knocked. No one answered. Then he pounded. Still, no one answered. Julyan had called Mary Jones a few days before to tell her he would be visiting. He continued pounding. The neighbors probably thought he was crazy. Finally, Jones opened the door.

Loud noises boomed from the TV. As Julyan walked into the apartment, he saw trash on the floor, flies in the kitchen, and dirt ground into the yellow shag carpet. He could smell rotting food and garbage simmering in the heat. The paint, grimy from neglect, peeled off the walls. Dirty palmprints lined the walls at waist level where Jones, a blind, elderly, homebound woman, braces herself to maneuver around the apartment.

PHOTOGRAPHY | C.E. MITCHELL

It was similar to culture shock. Julyan had not expected to see Jones, or anyone, living in these conditions.

After sitting down at the rickety kitchen table, Julyan asked Jones some questions about her life.

"Huh?" or "What?" was the common response.

Julyan would ask again.

"Huh?"

It soon became clear that Jones' hearing aids weren't working. Julyan spent the next two hours screaming at an old woman. It wasn't exactly what he thought it would be like when he'd signed up for Geriatric Experiences for Medical Students (GEMS), a program that pairs students from the University of Pittsburgh School of Medicine with mostly homebound elderly patients.

And then there was another miscommunication that had nothing to do with her hearing. Jones had lost her sight because of glaucoma about five years before. She thought that Julyan was going to examine her eyes and, perhaps, restore her sight.

At first, Jones barely showed any interest in Julyan. He was just another person showing up at her door, another person who couldn't help her see. A lot of characters—nurses, doctors, cleaning people—came in and out of her life. She wasn't quite ready to talk with this new guy. But after several visits, Jones felt she could trust Julyan and started to talk to him. Mostly Jones complained: about her neighbors—she was convinced they were selling crack; and her family—they were stealing her money; and her doctors—they didn't deserve to have degrees because they couldn't cure her blindness.

Even though Jones spent the first visit giving short answers and grumbling, Julyan left her apartment determined to help her. He knew he wasn't qualified to treat Jones, but he could try to get her placed in a safer environment. The dilapidated staircase could cause a serious fall. And it probably wasn't healthy to live in that waste. Julyan approached Andrea Fox, the faculty adviser for GEMS, explaining that Jones was in a dangerous situation; she would be safer and probably happier in an assisted living facility, Julyan thought. Besides, why would anyone want to live like that? He called Jones' home healthcare nurse with the same concerns. The nurse said Jones could make her own decisions. Fox agreed.

Fox explained to Julyan that he can't just take Jones out of her apartment. Jones wants to live there; and though she is a disabled elderly woman, she is competent and has a

right to manage her own life.

Two years later, Julyan recalls that first encounter with Jones. He had joined GEMS after hearing Fox talk to his class. GEMS is one of several "buddy" programs at the School of Medicine—including OPALS, which pairs students with children who have cancer; PALS, which pairs students and teen mothers; and now SHADOW, which pairs students with homeless people. Like the other programs, GEMS gives first-year students, who spend a lot of time mired in books, the chance to meet patients and form a significant social relationship with them, giving students an in-depth perspective on doctor-patient relations.

"A lot of students forget what they are here for. There's a lot to learn, and they become detached from patients," Fox says. "Medical education is reductive—you learn about cells, then an organ. You don't get to experience a whole person until you see someone in the hospital."

And GEMS, as well as other buddy programs at Pitt, does more than offer students an opportunity to interact with a patient as "the whole person." They often get med students out into the community to learn about the practical problems patients and their families face.

Fox's own experiences caring for older adults started when she did house calls during medical school at Boston University through a social medical program at her school. She'd found she particularly liked talking with older patients whenever she was upset or feeling a lot of stress. At Pitt, Fox, who is now an associate professor in the Division of Geriatric Medicine, regularly works with elderly patients. In 1997, she explored the idea of a mobile clinic in a van. That way, at least one day a week she could work in the community, and many homebound patients in underserved areas would have access to care. After a year, the van started doing rounds in the Hill District and Homewood; now it also serves the White Oak community. As Fox developed this Veterans Affairs-sponsored program, one of her students noticed that many of the elderly patients she talked to were lonely and depressed. The student suggested starting a group that gave medical students a chance to get to know elderly patients—hence GEMS.

Julyan recalls sitting in his doctor-patient relations classes. Over and over, he would hear that where people live affects how they care for themselves. He could never figure out how people's houses could affect their health. Then he met Jones; he saw that her stairwell ham-

pered her ability to leave her house, whittling away at her social life and mental health. The mess in the apartment also introduced hazards.

Fox urges GEMS students to investigate a number of issues that the elderly face when it comes to care. Yet Fox starts with the basics. The first task she asks students to complete: Call the patient. "They're learning how to talk to strangers," Fox says of students. "I want them to make their own discoveries."

Each month, Fox gives students another assignment, ranging from completing a functional assessment to, finally, taking vital signs—the task that seems to be the most difficult. Suddenly, the student must try to examine a friend.

The more Julyan visited Jones, the more she seemed interested in befriending the young man. And the more Julyan learned about her situation, the more he worried. People were breaking into her apartment, splintering doors, shattering locks. They even cut holes in the walls when they couldn't break through the door—all to steal her medication and Social Security money.

"It was hard for me to accept that someone was living in that type of condition," Julyan says. "You want what's best for elderly people. You want them to live in a place that's safe, you want them to have good treatment to help them out; and, as a doctor, that is what you would want for your patients, as well."

Jones chose a life that was arguably unhealthy—she lived in an unsafe neighborhood and in a hazardous and filthy apartment. She could barely walk with her cane, limiting her contact with others. But, as Julyan learned, even though her lifestyle prevented her from getting the best care, the important thing to Jones was that she was controlling her own life.

On one of the last warm days of a long Indian summer, first-year medical student Brian Miller hopped into his Jeep to drive to Earl "Mince" Mincemoyer's home in a southern suburb of Pittsburgh. He had a sheet of functional assessment blanks to fill in, but during the drive, Miller started thinking about other things he wanted to know about Mincemoyer. For one, Miller, as a Mennonite, didn't have any veterans in his family, and Mincemoyer had been a scout during World War II: *Did he have permanent damage from the frostbite he'd suffered during the war?*

"Hey, guys, how are you?" Miller asked as he walked through the door, passing Denise Advent, a home healthcare aide.

Mincemoyer pushed himself out of his new chair to greet him. (Mincemoyer later showed Miller how, with the push of a button, the seat



will lift so high that its occupant ends up standing.) Miller plopped down in the chair facing Mincemoyer and started asking him about big bands. Since learning that Mincemoyer has played in several, Miller has researched the music.

"So you play all the brass instruments and stand-up bass?" Miller asked Mincemoyer, who was a band director for 36 years.

"When I perform, I prefer brass, but I had to learn how to play woodwinds, too," Mincemoyer explained.

In between talking about big bands, Mincemoyer's experience in the service during World War II, and wondering what happened to the Steelers, Miller asked questions about Mincemoyer's ability to get around—does he dress himself in the morning? Can he shower? How does he get in and out of bed? Sometimes the transitions between casual conversation and Mincemoyer's ability to get around weren't smooth; Miller kept trying. He needed the information for his functional assessment, but at the same time, he was really interested in Mincemoyer's life stories and thoughts. He jokes

later that the reason he thinks the program is called GEMS is because he gets to meet a "gem" like Mincemoyer.

Advent, who has been Mincemoyer's nurse for the past three years, said in front of the two men during their visit, nodding toward Mincemoyer: "For two days, he has been saying, 'You know, he's coming at 2.' He likes Brian."

"Ah, I don't like him," Mincemoyer said. Then, with the wave of a hand, he made it clear he was joking:

"He's a very, very nice person."

As they chatted, Miller learned about Mincemoyer's history of heart attacks and strokes, which started in the 1960s. Mincemoyer mentioned how he always had a bottle of nitroglycerine close by, and Miller made a mental note to look up nitroglycerine when he had a moment.

"Pennsylvania 6-5,000," Mincemoyer chanted. "That's a very nice song."

"I thought you can't sing," Miller said.

"Naw." Mincemoyer's voice softened. His wife died recently in a bed in the dining

room—the room adjacent to where the two sat talking. As she lay on her deathbed, Mincemoyer held her hand and sang to her.

"I know she could hear me," Mincemoyer said.

"Yeah, she could hear you," Advent said.

Miller listened attentively to the exchange, nodding his head. He made another mental note to talk with Mincemoyer about death. He doesn't think that Mincemoyer is afraid of dying. Mincemoyer began saving money for his wife when he had his first heart attack in the late 1960s; he always thought he would be the first to go. Miller wonders how Mincemoyer copes with the recent loss of his wife.

Fox notes that though students are learning more about patients, they are not the only ones to benefit from GEMS. The older adults often gain a new sense of purpose because they are now, in a sense, teachers, helping to educate doctors.

Mincemoyer enjoys talking to his family and neighbors, but doesn't meet a lot of people. Through GEMS, a new friend came to him.

"One of the things you learn is how



Brian Miller meets with a "gem" of a new friend, Earl "Mince" Mincemoyer.

much of an impact you can make by stopping by, showing that you care. That means more than memorizing facts,” says Matthew Reese, who is cocoordinator of GEMS with Arvind Srinath. (Both students are in the Class of ’06.)

“This is the best day of my week,” Miller adds. “You can learn as much in this case as you would in the classroom.”

**C**ory Nordman kept losing. At first, he thought he was letting 11-year-old Billy Johnson win at Memory, a card matching game. After a while, the then-first-year medical student realized he was actually losing at a child’s game that required him to memorize pictures on a card. All that studying for exams must have hindered his ability to remember where the card with the kitten was.

**“You can only watch TV for so long. This is a new face who is interested in them and won’t do anything to hurt them—there are no needles.”**

After meeting Billy in January 2003, Nordman had been spending a lot of time in 8 North, a unit for cancer patients in Children’s Hospital of Pittsburgh. Billy had recently been diagnosed with osteosarcoma, a cancer that develops from the osteoblasts and affects mostly children and teens during growth spurts.

Nordman had spent a year between his graduation from Grove City College and his first year at the School of Medicine doing research at Children’s. At the hospital, he helped breed mice that were lacking a cancer-related gene as part of the lab’s research on leukemia. When he first heard of Oncology Patients and Loving Students (OPALS)—a program where medical students visit pediatric oncology patients during their stay at Children’s—he knew that he wanted to participate. Nordman wanted to see whom such research would help.

Whenever Billy is admitted to the hospital for a long stay, social worker Dennis Lee calls. That’s when the Memory marathons begin. Nordman will visit between classes and studying. If he is too busy during the day, he’ll stop by late at night. The nurses of 8 North know Nordman and let him peek into the room to check up on Billy and his mom, even though they’re often asleep by then.

Billy’s mom always stays with her son in the hospital. As soon as Nordman arrives,

she’ll pick up a book or leave the room to take a walk.

“Any time [parents] can be away and get outside of the room and sort of get some free space from a stressful situation, it helps them cope better,” Lee says. “Everything in their schedule is unnatural. It becomes something that is difficult to deal with at times.”

Both Billy and his mom seem excited to see Nordman. And just playing a game or watching a movie with Billy seems to comfort his whole family—especially the relatives who cannot always be at the hospital. They know that Billy’s mom has some support.

It’s almost as though Billy thinks Nordman is his age. As soon as his mother leaves, the normally quiet child starts chatting away, explaining to Nordman what chemotherapy drugs he is on, or explaining the details of his condition. As a student, Nordman isn’t sure if Billy is correct, until a nurse or a doctor comes in to ask Billy which drug

he has an adverse reaction to or if he had a particular x ray.

Billy also talks about camping and fishing with his family—how much he would rather do that than be in the hospital, but he rarely complains. Nordman is most surprised by how much energy Billy has, even though he is undergoing intensive therapy. The only time Billy ever stayed in bed, rather than playing Memory or video games or watching movies, was after he had some tumors removed.

“He knows when he’s in the hospital, I come; it’s one of the things he associates with being there,” Nordman says.

**T**hird-year Ryan LeVasseur started organizing OPALS after arriving at Pitt for medical school. LeVasseur was a middle school teacher and had worked at a home for abused children before deciding to become a pediatrician. As an undergrad at Georgetown, she participated in a program in which she visited children with cancer. The Jesuit priest who started the Georgetown program found that the relationship between the student and child helped boost the child’s morale and added to the patient’s overall health.

Once at Pitt, LeVasseur approached Kim Ritchey about starting a buddy program. Ritchey, director of hematology and oncology at Children’s, agreed to help. LeVasseur kept

busy her first year working with hospital staff to ensure the program would best serve the kids and their families. When LeVasseur started her second year, though she wanted to have a buddy of her own, she dedicated the year to helping other students find buddies.

LeVasseur asked students who were interested to submit an essay about why they wanted to participate in OPALS. She selected 14, then paired them with children who had either solid tumors or leukemia.

“We choose patients who are in the hospital a long time. They suffer from claustrophobia, hospitalitis, boredom, whatever,” Ritchey says. “You can only watch TV for so long. This is a new face who is interested in them and won’t do anything to hurt them—there are no needles.”

After a year, LeVasseur turned the OPALS reins over to Nordman, Heather Sanders, and Andy Beck, all now second-year students. Nordman and the others are hoping to expand OPALS.

“As more families learn about it, more are willing to join,” says Nordman.

But it is a slow process, and sometimes a student is without a buddy. So the coordinators hope to start a new volunteer program—sending buddyless students to talk with some patients in the ward. Also, Nordman, Sanders, and Beck hope to throw 8 North parties for patients and perhaps help the staff organize parties for the siblings who don’t have cancer so they can get some attention.

Participating students meet monthly to discuss their experiences with patients. (GEMS students do as well.) They also hear talks on hematology and oncology. Nordman feels lucky that he can see Billy throughout his whole treatment program; medicine has become so specialized, he notes, many doctors often see only one part of the process. He has learned that doctors can miss out on other things as well.

One day, as Nordman was sitting with Billy in his room, Billy’s doctor came in, explaining the latest round of tests. Billy and his mom listened, but became confused by what the physician was saying. When the doctor left, Billy asked Nordman what the doctor had said. Yet Nordman felt just as confused as Billy. As it became clear that the student was unable to clarify what they’d heard, Billy turned to him, making him promise that he would never talk like a doctor. ■

*Throughout this story, some patient identities have been obscured.*

*As we went to press, we were saddened to learn of the death of the boy we call Billy Johnson in this article.*




 A fluorescence micrograph showing several chondrocytes (cartilage cells) against a black background. The cells are stained with three different dyes: blue for nuclei, red for cytoplasm, and green for the extracellular matrix. The cells are irregular in shape, with some appearing as small clusters and others as elongated, spindle-shaped cells. The green staining highlights the dense network of collagen fibers surrounding the cells.
 

# RESISTANT TO DAMAGE

ON CONQUERING ARTHRITIS

AND OTHER BATTLES

BY DOTTIE HORN

ABOVE: The key to avoiding osteoarthritis is keeping these cartilage cells, called chondrocytes, healthy. Constance Chu has devoted herself to finding treatments to deter the debilitating disease.

It was Constance Chu's first day as a new cadet. Her hulking first sergeant lined up his company—all men except for Chu. The United States Military Academy at West Point had opened its doors to women three years earlier. The sergeant's voice boomed: "If you want to get through these Beast Barracks in plebe year, you have to walk, talk, look, think, and act like the man next to you." He strode up to the lone woman in his ranks. "Miss, what's your name?" he said.

"New cadet Chu, sir."

"Chu? What kind of name is that?" He turned away from her and then came back. "Well, I got news for you, Chu. I have a plane ticket home for you in my locker box anytime you want it."

It has been almost 25 years since Chu, now an assistant professor of orthopaedic surgery at the University of Pittsburgh School of Medicine, started at West Point. But even now, as the accomplished surgeon thinks back to those days, she pauses to compose herself before saying, in a level tone: "People told me every single day my first year at West Point, *We don't want you here. You will never make it. You can't do this.* And it's actually very emotional, because my gosh, when you're 17 years old, to have people say, *We don't want you here.* You have to dig deep and say, *I want to be here.*"

Chu, whose grandfather was a general in the Chinese army, became the first Chinese American woman to graduate from West Point. (Better, she ranked among the top 5 percent of her class in terms of cumulative military, athletic, and academic prowess.) If she had it to do over, she would, without hesitation, choose West Point again. The reason? "Because of that deep-down, gut-level absolute confidence that no matter what happens, no matter how dark it might look, I can do this."

Pretty much anyone with cartilage that's being worn away can be thankful for Chu's resolve. She's tackling osteoarthritis on a number of fronts, and won't let anyone tell her it's too difficult to advance the basic science behind the debilitating disease while also pursuing a demanding clinical practice. "As a surgeon, I love it when I see a patient who has a problem I can fix. As a basic scientist, the person who motivates me is the patient who comes in with a problem that I can't fix," says Chu.

But being well-known and respected within a community as an orthopaedic surgeon requires seeing a lot of patients. After all that time spent in the clinic and OR, there's little left over for the laboratory. With cutbacks in budgets at academic medical centers, there is often less money to support orthopaedic surgeons who want to pursue basic science. For these and other reasons, some of Chu's mentors discouraged her from pursuing her dual path. But Freddie Fu, chair of the Department of Orthopaedic Surgery, was impressed by Chu's unusual background and

her work on cartilage—leading him to recruit her while she was a fellow at Harvard University (where she was encouraged by Henry Mankin, MD '53). "She knows what she wants to do," says Fu. "She is also in a very hot research field—cartilage. She's definitely out of the box. I think she's outstanding."

After joining the Pitt faculty in 1999, Chu forged ahead with her professional plans, restricting her surgery practice to the knee so that she'd have more time for the lab.

"It's within my reach, doing basic science research to make a contribution that would impact many more people than I could personally treat myself," says Chu. She is ever mindful of those who suffer from arthritis, particularly the millions who can't find relief from current treatments.

**T**heresa Lach burst into tears the first time she visited Chu at her clinic. After teaching special education students for three decades, Lach, who was approaching retirement age, had stopped teaching because of the pain in her knees. The

prior joint injury.) For Lach, whose joint was destroyed by the disease, a knee replacement was a good option. Lach had the operation on her left knee in March 2003 and is glad she did; she is able to stand longer and walk farther than before, though she still has arthritis in her right knee.

But for others with end-stage arthritis, a total joint replacement is far from optimal. An artificial knee, which is made of metal and plastic, lasts about 15 years. As it wears out, bits of the synthetic material break off. Immune cells respond to the synthetic particles by attacking the bones to which the knee is attached and killing the bone cells. When the first knee wears out, doctors can often replace it again. Eventually, however, so much leg bone is destroyed that it is impossible to put in a new knee. A knee replacement is ideally suited for someone who is 10 to 15 years from the end of his or her expected life span.

But increasingly, arthritis is affecting younger people. One reason may be the growing corps of women participating in sports. Research suggests that the female

## More and more, orthopaedic surgeons are encountering patients in their 40s with end-stage arthritis in their knees.

four-minute walk from her car to the school building had become a struggle, and once inside, she had another 10-minute walk to reach her classroom. But retiring was not easy. "I was emotionally a wreck," says Lach. "I really liked my job, and I thought I could have put in many more years."

Throughout the previous decade, the pain in her knees had gotten progressively worse. A year before she retired, her left knee had buckled inward, and she was unable to straighten it.

Her knee problems affected most areas of her life. Lach loved to cook, but standing in the kitchen to prepare meals took her three times longer than before—she had to keep stopping to rest from the pain. "If I had to stand in line in the grocery store, it was excruciating," she says. "It was emotionally draining to be in constant pain. You lose all joy for life."

Lach is one of 21 million Americans who have osteoarthritis, arthritis that results from cartilage becoming frayed and worn. The incidence of this disease is expected to rise as the baby boomers get older. (Osteoarthritis is associated with age, as well as obesity, and a

knee—perhaps because of gender-based differences in training or a different anatomy—is more susceptible to injury than the male knee. Another contributing factor may be the epidemic of obesity in the United States.

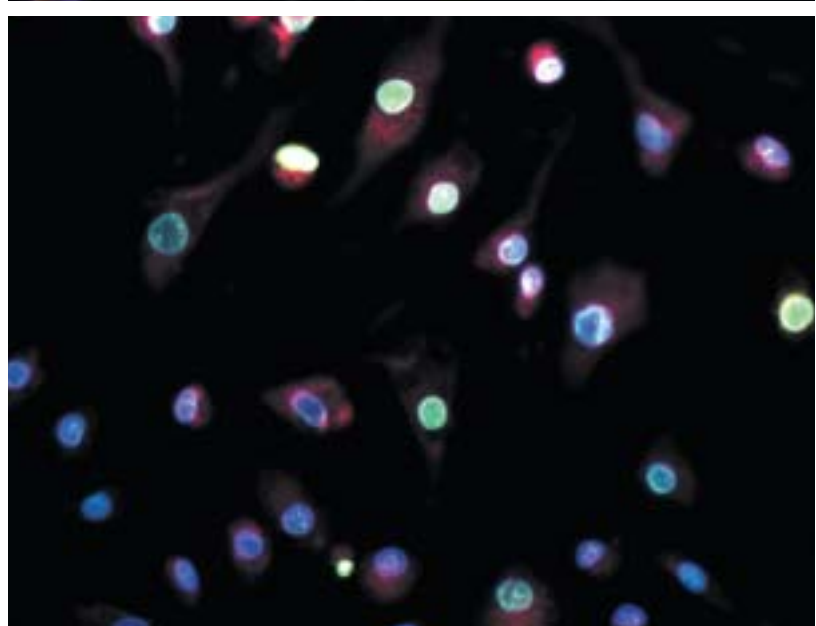
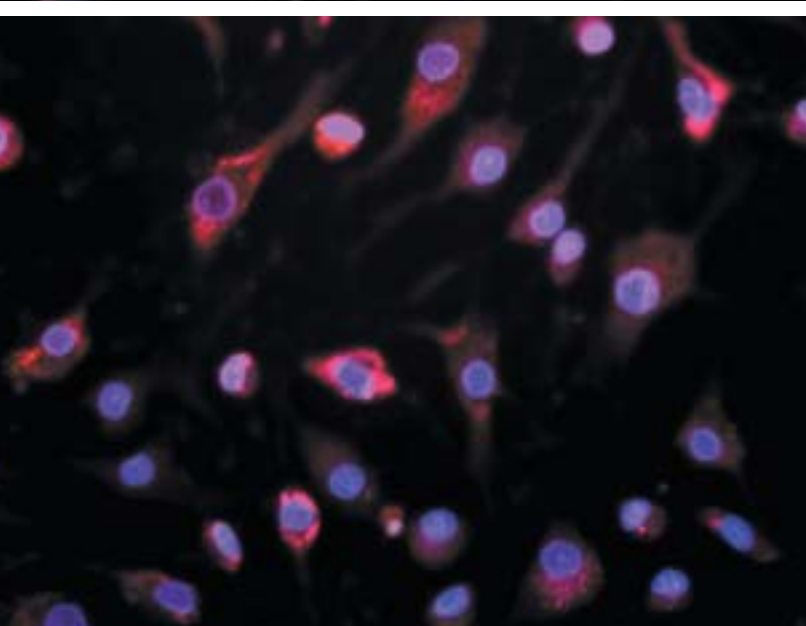
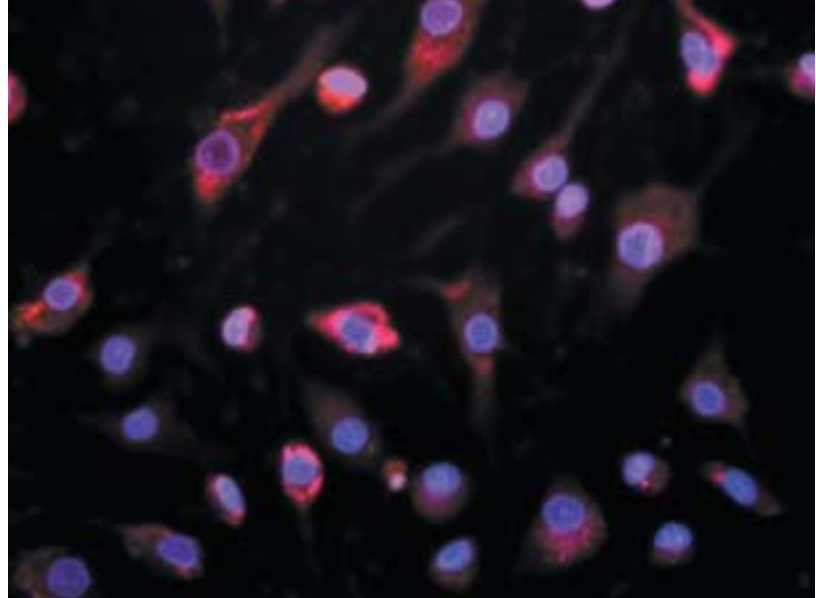
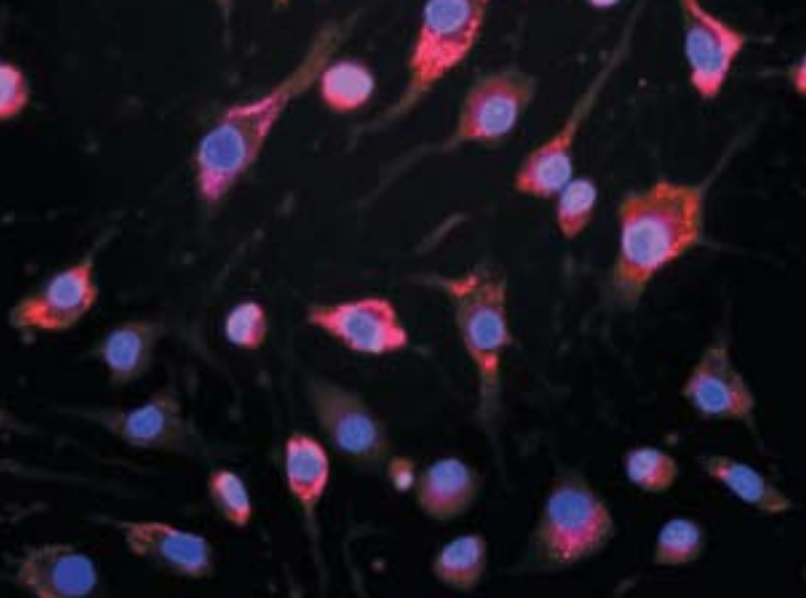
More and more, orthopaedic surgeons are encountering patients in their 40s with end-stage arthritis in their knees. "I have replaced knees in people as young as 40," says Chu. She tells young patients considering total joint replacement surgery that they could be in a wheelchair or lose a leg by the time they're 65. Chu won't perform a knee replacement in patients that young unless they're severely debilitated. "When you see that, it makes you more determined to find something for the 22-year-old who comes into your office, who has twisted a knee or had an injury, so that [he or she doesn't] show up at age 40 needing a knee replacement."

**W**henver two bones meet, cartilage at the end of each bone cushions the junction. The cartilage, which has a slippery surface, allows the ends of the



Anyone susceptible to osteoarthritis (which is an increasing fraction of the American population) can be thankful for Chu's resolve. She's shown here relaxing at home with Sid.





COURTESY C. CHU

**Using heat and other stress tests, Chu looks for ways to help cartilage cells survive injury. UPPER LEFT: Healthy cells at normal body temperature. Then Chu turns up the heat. UPPER RIGHT AND LOWER LEFT: At 113 degrees Fahrenheit and hotter. LOWER RIGHT: By 140 degrees, the cells are most likely dead. Their nuclei (formerly blue) have turned greenish-white, indicating that the cell's membranes are no longer working normally; most of their mitochondria (stained red) can no longer be seen, because they're not functioning.**

bones to glide smoothly over each other. Cartilage is 10 percent cells and 90 percent matrix (water and proteins secreted by the cells). It is the matrix that gives the cartilage its characteristic glassy smooth surface, stiffness, and ability to absorb shock. The cells, scattered here and there throughout the matrix, are like custodians: Their job is to renew and sustain the matrix. These specialized cells, found only in cartilage, are called chondrocytes.

The sudden impact of an injury or the chronic stress of excess weight can kill or damage chondrocytes. Instead of maintaining the matrix, an injured cell may release chemicals that break it down. Or the cell may simply die and be unable to perform its usual role. Once chondrocytes are dead or dysfunctional, there is nothing to renew the matrix. Little by little, over the course of years, the matrix wears away. The joint may become stiff and painful. Eventually, there will be no matrix left, and the ends of the bones will scrape against each other when the joint moves. This is end-stage arthritis, a realm in which debilitating pain like that experienced by Lach is the norm.

The degeneration of matrix causes arthritis and makes it an often silent disease as it encroaches. Let's say a rugby player is tackled, propelled into the air, and lands on her knee. She immediately suffers from pain and swelling in the joint, but in a few weeks, her knee feels fine. Yet inside, chondrocytes may have died, setting in motion the silent, decades-long breakdown of matrix.

Chu wants to know if there is a way to make those chondrocytes heartier, more likely to recover and become normal again after they are damaged. She has received a developmental National Institutes of Health grant to pursue this question. In the lab, Chu grows chondrocytes in small glass containers. First, she takes the chondrocytes and exposes them to stress—simulating an injury to a joint. One of the stressors she uses is interleukin 1, which is produced by cartilage cells in an arthritic knee. Chu is studying the effects of a number of substances that she hopes will protect the cells. She's hoping to find compounds that allow more cells to survive and preserve their ability to sustain a healthy matrix. Although she does not yet have definitive results, the studies are encouraging. For example, it appears that the COX2 inhibitors, anti-inflammatory drugs currently used to treat arthritic pain, do improve the ability of the cell to maintain the matrix. Chu wonders, if the drugs were administered in the early stages of the disease, before symptoms ever occur, would they help



prevent the breakdown of matrix?

She is one of many scientists seeking ways to make cartilage more durable. "There are many drug companies and biotech companies that are interested in developing drugs, or biologic agents, that protect the cartilage from damage or that accelerate repair processes," says John Klippel, president and CEO of the Arthritis Foundation. "So, we do believe that in the future, it's quite likely we're going to see drugs that are called chondroprotective drugs."

Let's say such a class of drugs were developed and our rugby player came into Chu's office shortly after falling on her knee. Chu knows she's at risk for developing arthritis, but there's no practical way to assess, for example, what percentage of the chondrocytes in her knee are dead or injured after the fall. The only way to get detailed cellular information would be to biopsy the cartilage. But that

moved it, and sometimes lock unexpectedly.

To repair an isolated defect like a "pothole" or a dent, orthopaedic surgeons have several options. One is to use cartilage from human cadavers to fill in the damaged area. As a resident at the University of California, San Diego, Chu studied patients who'd received knee cartilage transplants; she followed them for up to 10 years after the procedure. She found that 75 percent of the patients showed improvement in knee pain and function. In her study, the cartilage was transplanted after testing showed that it was not infected with bacteria or viruses—but it was always transplanted within three to seven days after the donor died.

Based in part on Chu's studies, tissue banks began offering cadaver cartilage for sale. One problem: Tissue banks take three weeks to complete the testing that ensures the carti-

chondrocytes derived from stem cells. She takes stem cells from human bone marrow, treats them with growth factors in the lab, and turns them into cartilage. For her studies, she uses rats that have been bred so that they will not generate an immune response against human cells. She makes a hole in the cartilage in the rat's knee. She then implants her lab-generated cartilage into the hole. After eight weeks, she has found that the implanted cartilage is still alive and is helping to repair the defect in the knee. When compared to rats that received the knee hole but not the implant, the implanted rats show less evidence of arthritic changes in the cartilage surrounding the hole.

While such results are promising, there are challenges to overcome before a similar treatment might be used in humans. Chu and others studying stem cells can generate enough cartilage to patch up a tiny rat knee.

But so far, no one has been able to grow a piece big enough to, say, fill in a big defect in a human knee. Normal cartilage is firm (firmer than garlic, says Chu), but a large piece of cartilage derived from stem cells is so soft

it often can't stand on its own. Lab-made chondrocytes don't organize themselves into the structure of natural cartilage. And as the Arthritis Foundation's Klippel notes, "One wants the cell produced [to be] as identical as possible to a normal, healthy human cartilage cell in terms of how it functions and the products it produces."

Chu will keep at it. After all, this was the woman who chose West Point over Stanford and Harvard. (She calls that choice a "no-brainer" because she thought that West Point would be a more well-rounded experience.) Chu is not one to be dissuaded—unless Valerie Brisco-Hooks is involved. Growing up in Los Angeles, Chu wanted to be a track star. She was the fastest runner in her elementary school. But there came a day when Chu's track dreams came to an end. Up until that point, she'd won most of her races. But one day in high school, Chu was the final runner in a relay and had a nice lead. Then, a girl she didn't know (Brisco-Hooks) came up from behind and passed her, winning with a huge lead. "She didn't just beat me. She creamed me. So at that point, I definitely knew: She's a track star. I'm not," recalls Chu. "I didn't quite recover from that until the 1984 Olympics, when Valerie Brisco-Hooks won the 200- and 400-meter gold medals." ■

## **One problem: Tissue banks take three weeks to complete the testing that ensures the cartilage is not infected. Chu has shown that after three weeks of refrigerated storage, all the cells are dead.**

would cause further damage to the joint.

So Chu and colleague Yingtian Pan have modified the minimally invasive surgical tool known as the arthroscope. Normally, it is inserted into a joint through a small tube, allowing the surgeon to see and do surgery inside of the joint. Chu and Pan have added optical coherence tomography to the arthroscope, enabling them to see what's happening at the microscopic level without damaging the cartilage. Chu has recently published two studies that show that the images obtained using the modified arthroscope provide the same detailed information you would get if you did a biopsy and then examined the tissue under the microscope. The new device may allow doctors to diagnose arthritis years before symptoms arise. If treatments are developed, doctors could then administer them to patients early—and hopefully slow down or prevent the progress of the disease.

**F**or some people who develop arthritis, there is nothing silent about the onset of the disease. If a man were in a car accident, for example, and his knee were propelled into the dashboard, the force of the impact might dent the cartilage. It's likely that bits of cartilage would then begin to flake off. The knee would hurt, swell, click when he

lance is not infected. Chu has shown that after three weeks of refrigerated storage, all the chondrocytes are dead. She now limits her use of the procedure and counsels patients that grafts from tissue banks will deteriorate over time. But she hopes to identify substances that, if they are placed in the storage fluid, might help chondrocytes survive. Her research suggests that, even if only 50 percent of the cells were alive at three weeks, the matrix could be maintained.

Another option for repairing an isolated defect is to take a biopsy of the cartilage, extract the chondrocytes, grow them in culture until there are millions of cells, and then re-implant those cells at the site of injury. This procedure results in improved function (though not a perfect knee) in about 75 percent of patients. Yet it is an appropriate therapy only for patients with small, discrete injuries. "I can only take a little bit of cartilage out of a person's knee, about 200 grams, and that's about half the size of a thumbnail," says Chu. The chondrocytes in the extracted cartilage can be induced to divide only a certain number of times before they will cease being chondrocytes. So, the number of cells that can be generated for repairing the defect is limited.

In the hope of overcoming this problem, Chu is exploring the possibility of implanting







AND HOW PITTSBURGH MAY BECOME THE SAFEST  
CITY AROUND WHEN IT COMES TO BIOWEAPONS


BY CHUCK STARESINIC

# LESSONS FROM A DARK WINTER

**A**t first, relatively few people heard about what happened during a simulated smallpox outbreak at Andrews Air Force Base in the summer of 2001. And for the most part, those who heard about it were not terribly alarmed. After all, it was just a simulation.

But that was before September 11. That was before weaponized anthrax had wafted out of anybody's mail. Immediately after September 11, the events of those two days at Andrews quickly began to take on ominous, portentous, mythical proportions. Lower Manhattan was still smoldering when Vice President Dick Cheney saw the videotapes himself and requested a briefing on the biowarfare exercise called Dark Winter.

ILLUSTRATION | DAVID POHL



**D**ark Winter was conducted entirely at a long conference table anchored center stage in the pit of an indoor amphitheater. The space was lit as if for a Broadway play. Several dozen observers who worked in public health or national security watched quietly in the darkness enveloping the stage. At the table sat an assortment of highly placed federal employees and public servants, past and present. The departments and agencies they represented read like a roll call of who might respond to a national crisis: Justice, Defense, State, Health and Human Services, FEMA, CIA, and FBI.

When everyone was assembled, a man in the role of the national security adviser said, "Before we begin this evening, I think it is important that you see what is currently on the local TV station in Oklahoma City. The White House Press Office just sent this over. I am sure this will soon be picked up by the major networks. This was taped from a live broadcast about 15 minutes ago."

All eyes turned to a large screen where a woman, apparently a television newscaster in Oklahoma City, looked into the camera and told the audience about "an outbreak of a mystery sickness." The level of tension in the room rose perceptibly with this video clip, the first of several to show how a biological weapon was unlike anything America had experienced to that point. A heightened sense of reality and urgency began to pervade the meeting as the camera cut to a man with a microphone standing outside a hospital, saying, "Sheila, off the record, doctors suspect that at least five patients at Southwest may have smallpox. Now that's a deadly virus not seen in this country for at least 20 years, so if it proves true, we could have a serious health emergency on our hands."

Former Senator Sam Nunn, presiding over the meeting in the role of the president, announced that one hour earlier, the Centers for Disease Control and Prevention (CDC) confirmed the presence of at least one case of smallpox and perhaps as many as 20 in Oklahoma City. Furthermore, he said, since smallpox no longer exists in nature, it is assumed that this is a deliberate bioterrorist attack. "A large proportion of the world population is now susceptible to smallpox," he said. "If this situation is not handled correctly, we could be facing the beginning of a nationwide or global epidemic."

Then-Governor Frank Keating of Oklahoma, who was at the table, asked for assurances that every one of Oklahoma's 3.5

million residents would receive the smallpox vaccine in the next 72 hours. It was an understandable request, but was there enough vaccine? There were only 12 million doses in a nation of 280 million, and what if smallpox showed up in other states tomorrow? Even if enough vaccine were available, what agency was prepared to conduct mass vaccination at high speed? Vaccination options would be presented for decision shortly, but first, an expert in infectious diseases presented relevant facts about smallpox. (Though the outbreak scenario is fictional, the following facts are not.) The last recorded case on the planet was in 1978. Routine vaccination against smallpox ceased in the United States in 1972, so no one under 30 is vaccinated. Vaccination appears to wear off over time, so many of those vaccinated decades ago may now be susceptible again.

**S**ince being eradicated under a World Health Organization (WHO) program, the official repositories of the smallpox virus have dwindled to two: a Russian lab and the CDC. The reason that smallpox is still a matter of some concern decades after being eradicated can be traced to those frozen stocks of virus.

We now know that, despite signing the Biological Weapons Convention, the Soviet Union surreptitiously engaged in large-scale production of weapons-grade smallpox, employing thousands of scientists and technicians in breeding the most deadly strains of smallpox available to them. The Soviet program was able to produce 20 to 100 tons of smallpox virus each year that could be loaded onto the warheads of specially designed ICBMs. In a war of mutually assured destruction, smallpox-laden missiles would release enormous clouds of aerosolized virus over American cities. The first hints of this became known to American intelligence only in 1989, and despite the shock and outright disbelief of many in the intelligence community, extensive details from former Soviet scientists and a wealth of corroborating evidence has revealed it to be absolutely true.

The Soviet program has since disintegrated. The fates of the smallpox virus and the scientists who produced it are uncertainties. Any scientist interested in starting a smallpox production facility would require little more than \$200,000 worth of basic equipment, a competent colleague or two, and a thimbleful of seed virus long forgotten, tucked away in a freezer for scientific purposes, or spirited away

from the sprawling and neglected remains of the Soviet program.

Because the last case of smallpox in the United States occurred in 1949, very few Americans understand how dreadful the disease is. Smallpox killed an estimated 300 million people in the 20th century alone. It killed more people in Europe than plague. When introduced in the 16th century to what is now Mexico, it killed half of the Aztec population, 12.5 million people.

Infection usually occurs when someone breathes airborne virus. It is believed that a few particles of virus may be enough for the disease to take hold. There are no symptoms until seven to 17 days after infection, when fever and malaise develop, followed by the appearance of a red rash. Lesions appear in the patient's throat and begin leaking microscopic infective particles, which are projected into the air when the patient speaks, coughs, or breathes. Typically, the rash consists of tiny pimples, which quickly grow larger and form heads rigid with pus. They become very painful and disfiguring and can cover the entire body, becoming especially thick at the extremities—the face, inside the mouth, scalp, hands, and feet. Approximately 30 percent of those who contract smallpox will die. Those who recover usually bear terrible scars and may suffer blindness.

In the world of Dark Winter, information was incomplete and evolving, but decisions needed to be made quickly. Even the participants who were veterans of similar exercises run by the Department of Defense felt totally out of their element—they knew little about epidemics or public health. A few hours into the exercise, an update on the status of the epidemic revealed 20 confirmed cases of smallpox in Oklahoma City and another 14 suspected. In addition, there were nine suspected cases in Pennsylvania and seven in Georgia. Hospital workers were failing to show up for work after the rumors of smallpox began. CDC officials were en route to help all three states.

Then, an interruption: "Mr. President, we have a 30-minute video clip you need to see urgently."

On the screen was the familiar logo of the nation's most popular cable television news source displayed beneath an ongoing interview with a scientist billed as an expert on smallpox.

"The problem is, we don't have enough vaccine," he is saying.

"Enough for what... the U.S. population?"

"We don't have sufficient stocks to pro-





FROM LEFT: Tara O'Toole, D.A. Henderson, Thomas Inglesby

CAMIE WESA

protect the people of Oklahoma, Pennsylvania, and Georgia, much less the entire U.S. population."

"What does that mean?"

"It means this could be a very dark winter in America."

**D**ark Winter was intended to shock influential people in Washington by showing them a realistic and plausible scenario for which the nation was totally unprepared.

"It succeeded magnificently," says Tara O'Toole, one of the principal designers and organizers of Dark Winter.

O'Toole is a newly appointed professor of medicine at the University of Pittsburgh and the chief executive officer of the new Center for Biosecurity of UPMC. At Dark Winter's "hot wash"—a Washington term for the immediate discussion of first impressions—the participants seemed stunned. O'Toole recalls the deputy secretary of defense saying that for the first three-quarters of the exercise he felt very tentative in his decision making because the issues of biodefense were simply too unfamiliar to him.

Nunn gave testimony in Congress one month after Dark Winter, saying, "During my 24 years on the Senate Armed Services Committee, I've seen scenarios and satellite photos and Pentagon plans for most any category of threat you can imagine. But a biological weapons attack on the United States fits no existing category of security threats. Psychologist Abraham Maslow once wrote: 'When all you have is a hammer, everything starts to look like a nail.' This is not a nail; it's different from other security threats; and to fight it, we need more tools than the ones we've been using."

These are the exact sorts of results O'Toole and her colleagues were aiming for—increased attention to overall preparedness within government and the public health community to deal with not only smallpox but a wide range of agents likely to be used in a biological attack. From her point of view, a

biological attack is much more likely than a nuclear attack. Biological science has advanced so rapidly that it is possible to create highly dangerous agents that resist treatment, and even small subnational groups have the ability to mount such attacks.

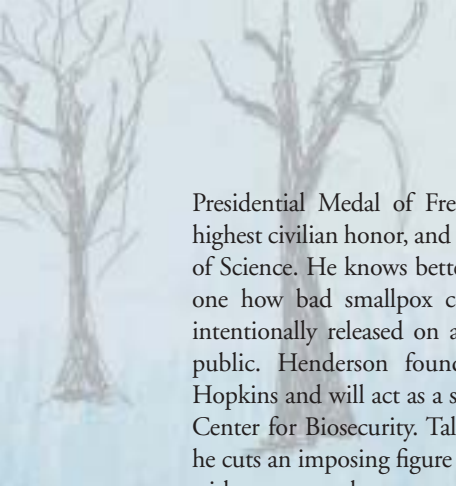
O'Toole is part of a small cadre of health professionals working toward better preparedness, and Dark Winter is just one of many bold steps they've taken in the past five years. The most recent came last September 17, with the announcement of the creation of the Center for Biosecurity of UPMC. That morning, the three leaders of the new center—O'Toole, Thomas Inglesby, and D.A. Henderson—sat down before a roomful of journalists and photographers. They then explained why they were dissolving the premier academic think tank on biological terrorism—the Center for Civilian Biodefense Strategies at Johns Hopkins University, which they had led since 1998. They were creating an organization with much broader capabilities. During the conference, O'Toole pointed out that the entire 20-person staff was making the move from Hopkins to the Center for Biosecurity. Eight, including herself, Inglesby, and Henderson, would have primary faculty appointments in Pitt's School of Medicine and secondary appointments in the Graduate School of Public Health.

It's hard to imagine three individuals whose words and actions have greater impact on the degree to which the United States is prepared for an act of biological terrorism. O'Toole is an occupational medicine physician who rose to director of the Hopkins center. She was formerly the chief safety officer for the nation's nuclear weapons complex.

Inglesby is an internist and an expert in infectious diseases and was the Hopkins center's deputy director. He has authored articles on anthrax, plague, and smallpox as biological weapons, in which he outlines how to manage cases and how the public health system might handle epidemics. Along with O'Toole, he was one of the principal designers of Dark Winter.

Henderson, the elder statesman of the group, is an epidemiologist who started working with the CDC in the 1950s and led WHO's successful global fight to eradicate smallpox. He is a recipient of both the

**"The real peril is going to emerge in three to five years, when advances in biotechnology and bioscience are going to make it possible to create even more powerful weapons."**



Presidential Medal of Freedom, the nation's highest civilian honor, and the National Medal of Science. He knows better than almost anyone how bad smallpox could be if it were intentionally released on a highly susceptible public. Henderson founded the center at Hopkins and will act as a senior adviser to the Center for Biosecurity. Tall and authoritative, he cuts an imposing figure and speaks at times with a measured sternness, though in conversation, he often reveals a more grandfatherly demeanor. He has tried to bring to a close several times his long career in academia and public service. Henderson was dean of the faculty of the Bloomberg School of Public Health at Hopkins from 1977 to 1990. He was science adviser to the first President Bush. During the Clinton administration, he was in the Department of Health and Human Services. He now serves as the senior science adviser to the Secretary of Health and Human Services and the Office of Public Preparedness.

He recalls the "major meetings" on federal preparedness in the 1990s: "There were no physicians, nobody in public health, nobody from a hospital, nobody from a health department. They were all police, fire, emergency rescue types, arms control people, and so forth. It was profoundly concerning."

Henderson thought that if he raised such issues, leadership would emerge, especially in academia, and he could move on to other things. He was interested in working on vaccines and other measures to combat naturally occurring epidemics in the developing world. When satisfactory leadership failed to emerge, he founded the Center for Civilian Biodefense Strategies at Johns Hopkins. He asked O'Toole to join him. She thought she was taking a temporary part-time job.

There should be at least three such centers around the country, Henderson has always believed. They would be affiliated with hospital systems that would serve as proving grounds for concepts and policies developed in the centers. But that failed to develop. "We had a whole day at Harvard and at the Kennedy School of Government," he said recently. "They came back a few weeks later and said, 'We don't have the expertise. We don't have the leadership.'" Henderson laughed, a bit incredulous, saying, "I thought if anybody could do it, Harvard could."

The decision to create the center at UPMC was made because, as O'Toole puts it, on September 11, 2001, the medical center here "actually started doing things." She cites some for-examples. Presbyterian has

sprinkler systems for chemical agents outside the emergency room. And an emergency room at UPMC St. Margaret is laid out to be able to deal with bioterrorism disasters. O'Toole sees UPMC as "one of the few truly integrated healthcare platform systems in America." She's attracted by its unusual communications capabilities, "like being able to talk to all of the doctors and healthcare personnel in an hour."

The center wants to collaborate with other efforts to make Pittsburgh the safest city around when it comes to biopreparedness, says O'Toole. And the city will serve the center's purposes by becoming "a template that can help the rest of the country become more secure," she says.

"We are going to try and create the model for how you would actually prepare hospitals to deal with a mass casualty situation. We're going to try and figure out how you would take care of people with a contagious disease in large numbers without having to shut down the hospital—as happened in a Toronto teaching hospital with only a few cases of SARS last year. We're going to try to figure out how to do mass immunization for a whole region in a matter of days. In a few years, Pittsburgh and UPMC will be seen as the Mecca for training for disaster preparedness."

**T**he first step to biopreparedness is to imagine bad things happening very vividly and realistically, says O'Toole, adding that not everyone can do so and stay sane. The key is to follow through with the second step—imagine the response just as vividly.

Take Michael Allswede. Bad things happen in his head all the time. Allswede is a former FBI SWAT team member; he looks like a football player in scrubs. These days, he's a member of the FBI's Joint Terrorism Task Force, cochair of UPMC's medical task force on bioterrorism, and a Pitt associate professor of emergency medicine. If you were to walk past Allswede on campus, he might be thinking about a patient in the ER or groceries he should pick up on the way home from work. But there's a significant possibility that he's visualizing a vast cloud of aerosolized anthrax wafting across a major metropolitan area.

To describe how UPMC is prepared to respond to such an incident, Allswede suggests drawing a time line and breaking it into five windows of opportunity, from pre-release to full-blown epidemic. Then lay out a slew of interventions; Allswede would scrawl acronyms in the margins and aim

them at the time line like alphabet arrows, each targeted to a specific window of time.

Some systems are running before a biological agent is even released. A network designed by Allswede allows any local doctor to consult with the strategic medical intelligence unit—a cadre of physicians around the region who are experts in infectious diseases, toxicology, and emergency medicine, all of whom are cleared to work on issues of national security. These volunteers help to determine if a given case might be the result of an attack and whether federal authorities should be called in to investigate further. The FBI endorses the effort, which has been put into play several times, during, for instance, Beaver County's recent hepatitis A outbreak.

But Allswede's world must allow for unlikely heroes and chance occurrences. Imagine, say, a curious Tom Sawyer-type who finds an abandoned, unopened sack of white powder and asks an adult, "What do you think this is?" Pitt researchers have an established relationship with the Allegheny County Health Department's new laboratory, which meets all federal guidelines for handling agents rated Biosafety Level 3 (BSL-3), several of which, like anthrax, are potential weapons. Thus, regional experts could conceivably identify the white powder and diagnose an attack long before symptoms appear. The School of Medicine will have its own BSL-3 lab in 2005 (see sidebar).

Drift back for a moment to the anthrax cloud wafting through Allswede's inner world. We may arrive around the middle of Allswede's time line with no Tom Sawyer, no sirens blaring, only a slight rise in nonspecific flu symptoms and visits to emergency rooms. Even before hospital staff clearly identify the nascent epidemic, two tracking systems kick into gear. Real-time Outbreak Disease Surveillance (RODS), developed here at Pitt, automatically alerts public health officials that local physicians had a busy day yesterday; a sister system lets them know more people than usual bought toilet tissue, aspirin, and other products associated with flu symptoms.

Acting on this red flag, county health department and UPMC physicians decide to engage an online system called the Terrorism Response and Information Center (TRIC). This communications network reveals that about half of 20 regional hospitals are seeing a high number of nonspecific flu symptoms. UPMC South Side has four times the number of anywhere else. Somewhere in that vicinity is the epicenter of the outbreak, where scores of people came into contact with an unknown biological agent sometime in the past several days. TRIC locates individual patients with flu symptoms at regional hospitals





Michael Allswede

CAMIMESA

and alerts their physicians to the possibility of a biological weapon being responsible.

The first official diagnosis of anthrax comes when a spinal tap performed on a man with suspected bacterial meningitis yields cloudy fluid heavily populated with anthrax bacteria. The moment the diagnosis is made, new systems can spring into action. The STAT Medevac system of some 15 helicopters begins shifting antibiotics to the hospitals most in need. Ciprofloxacin has been stockpiled in large quantities, along with doxycycline and amoxicillin, which are effective against some strains. Had the agent been highly contagious, as smallpox is, a quarantine facility at UPMC Presbyterian is prepared to take 300 patients—the sort of influx that would shut down most hospitals.

At this point, the region is wrestling with a full-fledged epidemic. With health department, law enforcement, and government officials, physicians will coordinate their activities through an integrated command center supplying voice and video linkages among hospitals.

Where is that command center?

“Can’t say,” says Allswede without missing a beat. Each hospital, including UPMC Presbyterian, has a communications center within it. But all he will reveal about the central command center is that it is somewhere in the vicinity of Presbyterian; the layout is designed so that activity at the central command center will not interfere with the vital work of running the hospital.

When WHO officially declared smallpox eradicated more than 20 years ago, D.A. Henderson began to worry that his many dedicated colleagues who’d participated in the eradication had not received adequate recognition for their accomplishment. The team had managed to bring the estimated 10 to 15 million cases of smallpox occurring annually to zero in just 14 years. So Henderson made and sent, at his own expense, certificates inducting each participant into the “Order of the Bifurcated Needle,” complete with a symbol showing the two-pronged vaccination needle curled into the shape of the magic number: zero.

The journey from the magic number, achieved in 1978, to Dark Winter in 2001 has left Henderson quietly angry. He feels betrayed by both the Soviets who ran the weapons program and by the Department of Defense, which, after learning of the Soviet program, undermined a movement in WHO to destroy all remaining stocks of smallpox in Russia and the United States. The DOD has since created a monkey model of the disease using its frozen stocks and has continued studying smallpox.

The Dark Winter scenario ended after projecting the number of cases six weeks into the outbreak; but participants asked for longer-term projections. O’Toole estimated the darkness would extend well into spring, with 3 million infected, 1 million dead, and no end in sight. In 2001, 12 million doses of vaccine existed, most of which would turn out to be useless because of age and improper storage. After O’Toole and others briefed Cheney on Dark Winter in September 2001, new vaccine was ordered within the week. The United States now has 300 million doses, but that doesn’t mean it will be easy to stop an epidemic. Besides logistical barriers to widespread vaccinations, the vaccine can cause serious complications and even death in rare cases. And already, genetic engineering raises the possibility of vaccine-resistant smallpox.

“The real peril,” says O’Toole, “is going to emerge in three to five years, when advances in biotechnology and bioscience are going to make it possible to create even more powerful weapons.”

Henderson resists dwelling on whether the eradication he oversaw could have somehow been more complete:

“The world has changed. I think we really cannot plan to eradicate any organism now. I think we have to simply realize that we have threats, be they terrorists or mother nature—à la coronavirus [SARS]. We better be able to respond and be ready to defend ourselves. And we’re going to have to be much better prepared than we are right now.” ■

## SIDE EFFECTS

**Eighteen million federal dollars will support the construction of a School of Medicine laboratory dedicated to basic research into biological agents that terrorists might use—a sobering undertaking with a desirable side effect: Those same biological agents cause thousands of deaths every day in the developing world, so Pitt researchers will be developing treatments and vaccines to respond to an immediate need while they work toward greater national security.**

The Regional Biocontainment Laboratory (RBL) was awarded to Pitt in September by the National Institute of Allergy and Infectious Diseases (NIAID). It will occupy an entire floor of the new Biomedical Science Tower 3, and it will be unlike any other lab at the University. Extraordinary safety and security features that exceed federal standards for Biosafety Level 3 will allow Pitt to establish vaccine programs on diseases like anthrax, dengue, West Nile virus, encephalitis viruses, and hemorrhagic viruses. The CDC and NIAID are supporting research on these agents and others because they are the most likely to be weaponized. But as Arthur Levine, the primary investigator on the grant as well as senior vice chancellor for the health sciences and dean of the School of Medicine, notes, these biodefense dollars have the potential to make an enormous contribution to the global fight against these diseases, because these diseases have been largely ignored by another major source of research dollars—the pharmaceutical industry. “Merck and Pfizer, et cetera, can’t get rich selling vaccines in undeveloped countries,” Levine notes wryly. “They can only get sued.”

The RBL is expected to support two or three large Pitt research groups and to lead to multiple strategic new hires. It will be a national resource where vaccines against deadly diseases can be developed and tested before clinical trials. —CS

One scientist noted  
**the ubiquity of  
the protein's  
role in cancers** in the  
title of a recent  
paper: **“Is this  
the onco gene  
from Hell?”**



NOW, SMALL IS BIG | BY ROBIN MEJIA

# WHEN IT COMES TO CANCER, WHAT'S RATIONAL?

Not too long ago, doctors could basically describe a cancer by what they could see, albeit with the help of a microscope. In fact, cancers are named by the tissue in which they occur, not by the mechanism that makes cells proliferate out of control. Advances, especially in DNA technologies, have let researchers start to describe cancers at a molecular level. What they are finding is that existing classification schemes are inadequate. Tumors that appear identical by traditional measures may very well be caused by different molecular problems. The conventional classification system—identifying cancers by tissues—is sort of like describing car problems by make or model. If you were to tell your mechanic, “I’ve got a Toyota Camry that won’t start,” that’s helpful; Camrys are different from Chevy Suburbans. But your mechanic needs more information to get you back on the road.

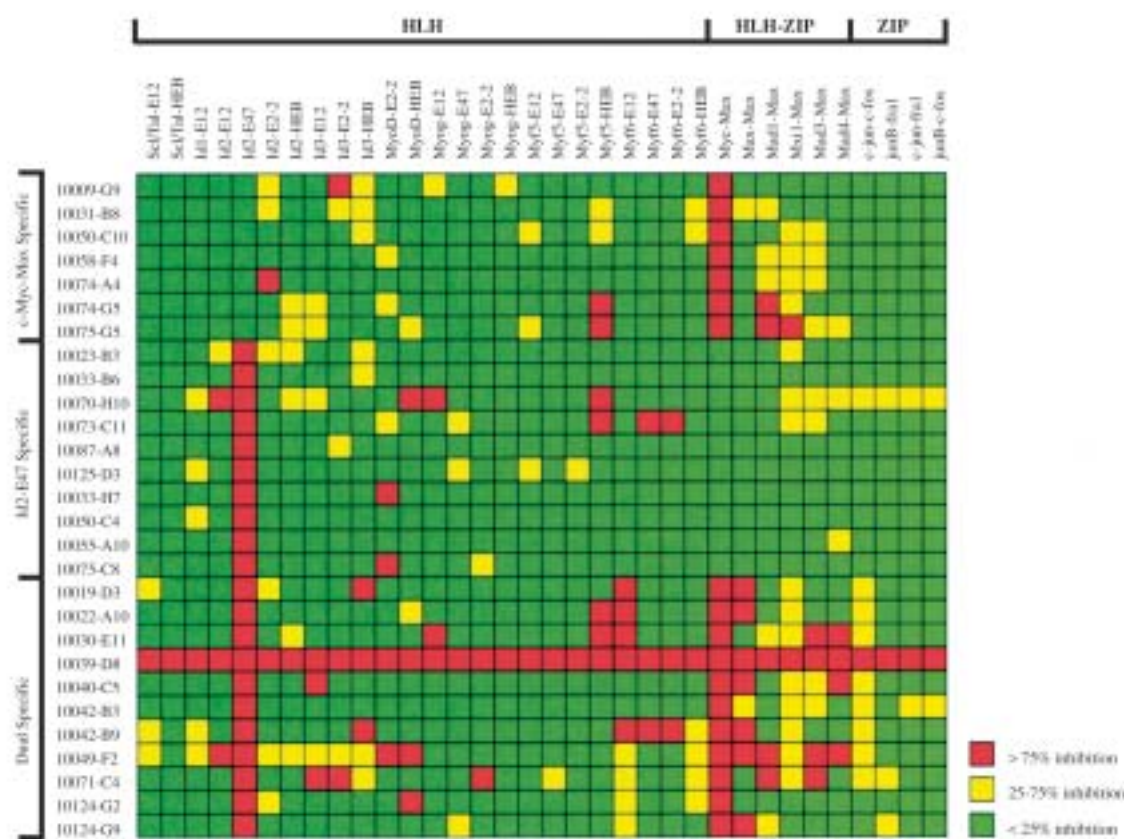
The smartest approach may be to, in essence, look under the hood at cancer. A better understanding of the molecular problems that cause cancer promises to explain why some tumors respond well to traditional therapy, yet other similar-looking cancers, treated with the same drugs, still prove fatal. Molecular information is helping researchers design drugs to target specific molecular actions. The research community has become so taken with this approach, they refer to the process as “rational drug design.”

The cancer drug Gleevec is the poster child for this kind of research. By targeting a specific protein mutation seen in patients with chronic myelogenous leukemia, Gleevec has offered rapid relief to patients. The drug kills tumors but doesn't go on a rampage, destroying lots of noncancerous cells, so there are few side effects. Its success has been remarkable and has spurred more research into targeted cancer treatments.

Last March, Peter Wipf, a professor in the Department of Chemistry at the University of Pittsburgh, contacted Edward Prochownik, the Paul C. Gaffney Professor at Children's Hospital and a professor of molecular genetics and biochemistry as well as pediatrics for the School of Medicine. Wipf asked Prochownik, an MD/PhD molecular biologist, to present his most current cancer research to a group of University chemists. In itself, the invitation might not seem like a big deal. After all, "interdisciplinary" has become a buzzword. But this meeting was the kind that reminds us why there's buzz in the first place: The collaboration it led to could have big payoffs. Wipf heads a program to build a University of Pittsburgh chemical library for drug development. It's one of only four such university programs in the country and funded by a \$9.6 million grant from the National Institutes of Health. Prochownik is pursuing new therapies to fight many common cancers. He is part of a class of cancer researchers poised to capitalize on the wealth of newly available information offered by genetics that may lead to rational designs. Both men are exploring the possibility of creating cancer-fighting compounds that are made from small molecules, like Gleevec is.

To backtrack: Gleevec can best be viewed as a harbinger of change. It zeroes in on a single mutation. Not all cancers are so easily targeted; so researchers study the genes and proteins involved in different cancers in order to determine the best points of attack. Prochownik has his sights set on a protein called "myc." Myc is involved in many cancers, including some common lymphomas and colon, breast, and prostate cancers. One scientist noted the ubiquity of the protein's role in cancers in the title of a recent *Cancer Cell* paper: "Myc—Is this the oncogene from Hell?"

Myc regulates more than 600 genes. And,



The top of the chart lists protein pairs that normally interact; the red squares indicate a disrupted interaction. The compounds Edward Prochownik and colleagues are studying stopped the interaction of myc and max (which is key to many cancers) but did not affect many other proteins. That's a good thing when it comes to drug development.

like so many genes that can promote cancer, many of these myc-targeted genes are essential to normal cell functions. In fact, so many of these genes are key to development that researchers cannot make a myc knockout mouse—that is, a mouse with the myc gene "turned off." When they try, the embryo dies. In adults, cells turn on myc production during differentiation and proliferation. These, of course, are the very activities that, in overdrive, can cause normal cells to go cancerous.

For a while, Prochownik had focused on strategies that could affect myc's target genes. Eventually, he realized that he needed to take a step back. Not only does myc regulate hundreds of genes, many of those genes seem to code for redundant functions. Even if he could inhibit one or a few of the targets he knew promoted tumor growth, other genes regulated by myc would still keep pumping out proteins. He started pondering how scientists could inhibit myc itself.

It would have been easier, or at least a more straightforward problem, if one single failure sent myc into overdrive. But that's not the case. Some breast cancer patients have 10 copies of the gene for myc. In other cancers, the gene gets transposed onto a section of the

chromosome that's heavily expressed. Other times, a protein that normally keeps myc production under control fails.

It became difficult to imagine a single drug that could manipulate myc under all of these circumstances. So Prochownik sought out another point of attack.

"When you look at a picture long enough, you start to see things," he says.

In order for myc to act on target genes, it interacts with another protein, one that scientists call "max." Without max, myc simply can't do its jobs.

"It became apparent that this interaction of myc and max might be its Achilles' heel," Prochownik says.

At first, Prochownik wanted to study potential drugs in mammalian cells. These cells are a complex environment. Many compounds that seem to work elsewhere fail in mammals. Any number of things can go wrong in the mammalian cell—drugs can't get across the cell membrane, they aren't soluble in the cell environment, they break down too quickly to have much effect. So Prochownik put together a team to develop a mammalian cell-based screening technique. The team of four worked on the project for a year and a half. They put



in a lot of hours. It amounted to, says Prochownik, a complete failure. By the end, he was nearly ready to throw in the towel.

However, the team had never tried using a simpler organism for an initial screening. That would still bring up the possibility of false positives—they might find chemicals that looked promising initially but couldn't hack it in a cell. But it seemed better than nothing.

"We'd put in so much time and effort, we decided it was worth a try," Prochownik says. After several months of effort, they could afford the days it would take to plate out a modified yeast strain and try to screen for myc-max activity. The first test took five days—and, to their pleased surprise, it worked.

The assay they developed offered a streamlined peek at the proteins' interactions. The assay had been engineered so that if myc and max interacted, the yeast made beta-galactosidase (a sugar). That sugar makes the plate turn brown. So if a compound disrupted the interaction, Prochownik's team knew, because the plate wouldn't turn brown.

With a test in hand, the researchers were ready to screen potential drugs. They just needed something to screen. Small molecules, or, more specifically, low-molecular-weight compounds, are attractive to researchers, as they can often be turned into pills fairly easily. Nucleic acids and proteins often disrupt interactions as well as small molecules do, but the human digestive tract is designed to break them down—nucleic acids and proteins are, after all, part of a well-balanced diet. (That doesn't mean they can never be used as drugs, but their administration tends to be trickier.)

John Lazo, chair of the Department of Pharmacology and a collaborator of Prochownik's, had a library of low-molecular-weight compounds from a chemistry supply company. The library was created for automated screens. During the testing, a robot takes a sample of one of the chemicals and adds it to the yeast plates. The researchers let the yeast grow for a bit, then check to see if the plate turns brown. If it does, they know myc and max are still interacting.

At its heart, the automated screening technique lets scientists facilitate serendipity. The researchers picked the interaction they cared about, but they didn't select the compounds that they thought were likely to affect myc-max interaction; they simply tested every small molecule in the chemical company's library—all 10,000 of them.

This kind of experimentation has been a part of cancer discoveries for years. Researchers

found many of today's chemotherapy drugs by simply testing whatever chemicals they happened to have on their shelves. Two things have changed, however. One is processing power. "Technology makes it possible for us to screen thousands of these compounds at a time instead of five or six," notes Prochownik. The other is specificity. Using their improved understanding of cancers, researchers are able to screen for specific properties—like whether a compound inhibits protein interaction—instead of simply throwing drugs at a tumor and watching to see if it shrinks.

In this case, the numbers game seems to be panning out. Of the 10,000 chemicals Prochownik's team screened, seven disrupted myc-max interaction.

**L**ike any single cancer drug, Gleevec has its limits. Already doctors are seeing cases of resistance in patients who've come out of remission.

"What you really need are very specific attacks targeted at multiple levels," says Prochownik. He envisions therapy regimens that involve multiple small molecule treatments, possibly in combination with other targeted approaches or traditional chemotherapy.

Another group looking at myc-max interaction has had some initial success targeting RNA to stop the interaction. If that group's research evolves into a therapy, Prochownik imagines it could be used alongside small-molecule drugs to attack a common enemy on different fronts. (The RNA studies are also in early stages, but Prochownik finds them encouraging. They show that inhibiting myc seems to make some traditional chemotherapy treatments more effective. And it appears that such treatments only need to be administered for short times to have these effects, an important consideration, given that myc is needed by healthy cells.)

Prochownik won't make predictions about how well the compounds he's discovering will fare as drugs. That's not to say he isn't optimistic—his laptop is loaded with myc-max slides, and he's writing a review article on the viability of myc as a target. But at 53, he has been in this game long enough to know the vast majority of compounds that look promising in early lab tests don't actually make it to pharmacists' shelves. Yet his work is moving ahead quickly. He's already studying his seven compounds in mice to see which, if any, the animals can tolerate. If the compounds stop myc in mice—without harmful side effects—he'll move on to Phase 1 clinical trials, the

first step in testing drugs in humans.

If you want to see Prochownik truly excited, ask about the value of the screen he has validated—the modified yeast assay he was so reluctant to pursue initially. Remember his (very legitimate) fear that what worked in a simple system might not work in mammals? It turns out he has found a simple system that is also a great proxy. Every molecule that affected myc and max in yeast has done the same thing in mammalian cells. This is no small accomplishment. It means that he can confidently use it to screen more compounds, which he'll be doing shortly. It also means other researchers looking at other protein interactions have a new tool in their box. The assay can be modified to screen for a variety of different protein interactions.

In addition to being good drug candidates, small molecules like those Prochownik's team have identified are particularly attractive for development. They are easy, and cheap, to make into drugs. And cost becomes important even in trials, long before drugs get to market. In addition, small molecules are easy for chemists to modify. That's where Peter Wipf and the Combinatorial Chemistry Center come in.

The chemical library Wipf is building is similar in concept to the commercial one Lazo purchased. But because it's being developed at Pitt, it will give researchers here an edge in drug development. The library will be available to all University researchers.

Wipf is now working with Prochownik and pharmacologists Lazo and Julie Eiseman, who is a research associate professor of pharmacology, to create derivatives of the compounds that have already been shown to disrupt myc-max interactions. Prochownik's team will then screen these likely candidates, looking for compounds that act even more strongly or specifically against myc and max. They'll be increasing their odds of creating a drug that will work in people. And, by studying which modifications make the cut, the team will be able to tease out more about how the molecules actually work.

"It's very promising," says Wipf, in terms of the fundamental knowledge about cell biology to be had.

"I think the future is one where we're going to be combining these kinds of targeted therapies with a molecular knowledge of the tumor," says Prochownik.

In this future, a breast cancer won't just be a breast cancer, it will be a cancer with a molecular profile, and treatments to match. ■



Freedom House Enterprises opened in the Hill District in 1967, planning to jump start businesses that would offer meaningful employment to this troubled community. Pretty soon, they were running one of the nation's most advanced ambulance services.

# SEND FREEDOM HOUSE!

**NOBODY HAD SEEN AMBULANCE  
ATTENDANTS LIKE THESE BEFORE**  
BY CHUCK STARESINIC

John Moon was a young paramedic eager to increase his professional skills and confidence when he walked into the emergency room at Allegheny General Hospital. He'd performed a physical exam on the patient en route from downtown. He'd even rehearsed presenting the patient to the emergency room staff until he had it down to a T—blood pressure, pulse, history, and more. At that time, in 1974, sophisticated ambulance service was practically unheard of. Throughout Pittsburgh and the entire nation, ambulance attendants routinely brought critical accident victims and the gravely ill to the hospital with little or no medical attention. Few people even knew what a paramedic was. Police officers with no specialized training and no equipment drove ambulances like they were driving delivery trucks,





**ABOVE:** Philip Hallen (left) helped bring Freedom House Enterprises together with Presbyterian-University Hospital and Peter Safar (right). **RIGHT:** Ambulance service staff shown clockwise from top right corner—Joe Hirsch, William Draper, Doris Owens, Nancy Caroline, Wilma Mosley, John Moon, John Bucci, and David Clemons.



and proper care generally began at the hospital doors, provided the patient was still alive.

Emergency medical technicians like Moon, working for the Freedom House Enterprises Ambulance Service, were the vanguard of change. Trained to exacting standards under the iron gaze of the University of Pittsburgh's Peter Safar, the Freedom House EMTs primarily served Pittsburgh's Hill District and Oakland from a base of operations at Presbyterian-University Hospital beginning in 1968. The vehicles they drove were designed to Safar's specifications and outfitted with EKG monitors, IV drips, intubation kits, blood pressure cuffs, and defibrillators. They looked more like roving exam rooms than the hearselike vehicles the public knew as ambulances.

Nancy Caroline went into the ER with Moon that day. She was a critical care physician at the University of Pittsburgh whom Safar had handpicked as medical director for Freedom House. In the ambulance, she had prepped and encouraged Moon. As they entered the hospital, a nurse came to help, and Moon launched into his presentation. Moon, in addition to being a Black man in a mostly White arena, personified the most advanced prehospital care available anywhere in the nation. The nurse, apparently unaccustomed to being addressed in this way by an ambulance attendant, laughed at him and walked away before he could finish.

Moon turned to Caroline and said, "This

went through that." Caroline looked straight back at him. Despite her gentle features and youth, she was tougher than nails on her EMTs. She was always watching them, listening to them on the radio, telling them how they could be better, how they had to be better. She was tough. She was their mentor. And they absolutely loved her for it. She replied, "If you don't learn to talk to the emergency room staff on their own terms and in their language, no one will ever listen to you." She wasn't letting him go anywhere until he did his job.

In 1967, Freedom House Enterprises was a fledgling nonprofit corporation in the Hill District trying to uplift the community by creating African American-owned businesses that would provide meaningful employment and job training. They started a service that sold fruits and vegetables out of trucks on the Hill. Philip Hallen, director of the Maurice Falk Medical Fund, figured if Freedom House could bring produce to a neighborhood that was lacking grocery stores, they could run a commercial service to transport people for hospital visits and routine checkups. Hallen introduced Freedom House board members to his former classmate from Yale, Ed Noroian, who was the director of Presbyterian-University Hospital. Noroian offered to house an ambulance service at Presbyterian, and he asked Safar to train the paramedics. At that point, an interesting idea blossomed into

is useless. I don't know why we even

a revolutionary one.

Safar was a consummate scientist and an uncompromising humanist. The anesthesiologist from Vienna had helped develop the formula for cardiopulmonary resuscitation and demonstrated that Boy Scouts and firefighters could be trained to provide basic life support. Now he wanted to demonstrate that sophisticated care administered by trained laypeople would save a great many lives. When Noroian approached him, he was already working on standards for ambulance attendants.

It was an audacious plan. Some would say ridiculous—a poverty program that would take unemployed people from the Hill District and train them to provide emergency medical care in the streets. The day before training began, Jim McCoy, the president and founder of Freedom House Enterprises, recruited people right off the street. Nearly half had not completed high school. Some needed help with basic skills like reading and math before more advanced training could begin.

In the hospitals, Safar and Noroian paved their way, instantly legitimizing the unexpected arrival of a few dozen African Americans in white uniforms. They wore patches that read "Ambulance Attendant Trainee." Their training far exceeded any existing standards—300 hours of classroom and clinical work in anatomy and physiology, first aid, resuscitation, medical ethics, and legalities. They did rotations in the operating room, recovery room, intensive care unit, morgue, emergency room, and maternity ward.

The first Freedom House ambulances hit the streets in the summer of 1968. By October, Safar was writing to the mayor, describing the success of the service and urging that Freedom House's contract with the city be expanded.

But despite its unqualified success in demonstrating and delivering cutting-edge ambulance care, Freedom House was in for a bumpy ride. It relied on grants, and financial stability was difficult to achieve. City police continued to run ambulances throughout the city, frequently rushing in to transport accident victims without any stabilization before Freedom House could arrive. Freedom House began racing police ambulances to the scene. Hallen says that racism prevented elements of the police and city government from appreciating Freedom House for the unparalleled asset it was.

One paramedic told filmmaker Gene Starzenski, who is producing a documentary on Freedom House, "We were determined to succeed because everyone told us we would fail."

Their successes were many, from small personal victories to individual lives saved, and, eventually, to the shaping of national standards.

A 1971 study found that 62 percent of patients received inappropriate care from the police, while 11 percent received inappropriate care from Freedom House. Eventually, police officers in need of an ambulance for themselves or a family member would call the Freedom House dispatcher instead of the police.

When Nancy Caroline came on as medical director in 1974, she instituted a rigorous system of monitoring, or, as she called it in *Pittsburgh* magazine in 1977, "an Orwellian reign of terror." She went on ambulance runs with the paramedics, even when she'd already worked so many hours that most people would have gone home. She monitored radio traffic and picked up the microphone at all hours to "question, chastise, harangue." Given a chance, she would catch a few hours of sleep on the cot in the ambulance.

John Moon says that Caroline was "warm, gentle, kind, and intimidating." She developed a close camaraderie with the paramedics, many of whom would have followed her anywhere. She made sure they got the training and support they needed. "There were many times," says Moon, "she'd be walking down the hall with five Freedom House paramedics



walking right with her, going into the ICU to look at a particular patient."

Caroline, who died of cancer in 2002, remembered with particular pride Moon's struggle for respect in the emergency room. Describing the scene in *Pittsburgh* magazine, she picked up the story after the nurse turned her back on Moon, writing that he then cornered the ER physician and with "military precision" said, "We have a 19-year-old man who experienced a dizzy spell without syncope while lifting some cartons at work. His past medical history is negative except for a heart murmur present since childhood. His pulse was irregular, ranging from 38 to 110, his blood pressure was 110/70 and his respirations 20. The rest of the physical exam was negative except for a short systolic murmur. His EKG shows evidence of bradycardia syndrome."

With a smile, Moon then handed the EKG strip to the physician and proceeded to help the nurses move the patient. Caroline said they laughed all the way back to Presbyterian.

In 1975, Freedom House paramedics presented a disaster drill for an international symposium on critical care medicine. They were judged among the most sophisticated and skilled in the nation. Drawing heavily on lessons learned with Freedom House, Caroline would go on to write *Emergency Care in the Streets*—for years, the only textbook for paramedics. Under Safar's direction, Freedom House EMTs tested and implemented the U.S. Department of Transportation's standards for ambulance training and equipment eventually adopted by 40 states.

In 1975, the City of Pittsburgh ended its

**From 1968 to '75, one of the safest places to be was in the hands of a Freedom House EMT. (Although the cat seems uncomfortable in the hands of Philip Hallen.)**

contract with Freedom House and instituted its own modern ambulance service—Emergency Medical Services (EMS), which exists to this day. There was anger and bitterness within Freedom House, whose paramedics were assured they could be hired by the city if they passed a test. Many felt that the city should have committed to expanding Freedom House into a citywide operation. One of the more outspoken paramedics was quoted in the *Pittsburgh Post-Gazette* saying, "If this was a mostly White organization, I don't think this thing would be happening."

About a dozen Freedom House paramedics did go to work for the city. John Moon is currently an assistant chief with EMS, and one of its longest-serving employees. Mitchell Brown moved from Freedom House to the city and is now public safety director for the City of Columbus, Ohio. Many pursued advanced degrees and careers in health services like these two. Some became unemployed or drifted back to unskilled work.

Philip Hallen notes that at a memorial service last year for Peter Safar, amid all the descriptions of his achievements, there was no mention of his work with Freedom House. John Moon still laments that the vast majority of paramedics, even in Pittsburgh, know nothing about Freedom House. He considers the organization one of the greatest blessings in his life. So would many others, paramedics and patients alike, if only they knew. ■



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



stomach cancer, he contacted a local physician who put him in touch with a doctor there. That was the start of a long correspondence and a fruitful relationship. Raizman now visits Northern India about every two years. (His audience with the Dalai Lama came

on the first trip.) Early on, he helped his colleague in the western-style hospital. Raizman personally donated an endoscope plus other equipment and supplies. Now that the hospital is running fairly well, he travels to more remote communities and refugee camps to provide care.

Raizman, a private-practice gastroenterologist and medical director of the UPMC Monroeville Surgery Center, sits on the School of Medicine's Board of Visitors. He was recently asked to be on the steering committee for the new area of concentration program in global health. AOCs give Pitt med students a chance to earn certificates in specific areas of interest; certificates are offered in seven areas, including geriatrics, women's health, and medical humanities. Raizman not only signed on to the global health steering committee, he donated seed money for the AOC and to support students interested in donating their time and skills in the developing world.

Students can grow in many ways by providing health care where it's so desperately needed, says Raizman. They can refine skills in physical diagnosis, because laboratory analysis and equipment are simply unavailable in hard-to-reach places like Northern India. Other effects of such experiences are more difficult to define, says Raizman, noting that his own sense of compassion has deepened. Working in India requires him to think less about peripherals like staffing and equipment and more about caring for patients—what's most important. It's never too early to learn such lessons, he says: "When we train young physicians, the perspective they have is the perspective that we give them."



A Tibetan community in Bir, Northern India

## THE ROAD TO DHARAMSALA

RAIZMAN'S WORLD VIEW  
BY CHUCK STARESINIC

**M**edical students who are wondering how to get from Scaife Hall to, say, the residence of His Holiness the Dalai Lama in Dharamsala, India, might start by talking to Richard Raizman (MD '71). He knows a bit about that journey. In fact, students interested in expanding their course of study to explore almost any country from Albania to Zanzibar will find support, encouragement, and a role model in Raizman.

A decade ago, Raizman knew little about Northern India or the 100,000 Tibetan exiles living there, but he knew gastroenterology. And when he learned that many Tibetan communities in India suffered a high incidence of gastrointestinal problems, including



Raizman (with beard) with colleague Tsetan Sadutshang (left) talking with a patient at a clinic in Bir

## BOOSTER SHOTS

**R**ecently retired Pitt neurosurgeon and clinical professor **Peter Sheptak** (MD '63, Res '68) could be excused if he seemed to celebrate Mario Lemieux's goals more than most. The Pittsburgh Penguins star center twice had back surgery performed by Sheptak, the team neurosurgeon. In addition to being an irrepressible sports fan, Sheptak was known on campus as a major teaching influence in the Department of Neurological Surgery for more than 35 years. His colleagues have initiated a campaign for an endowed chair in his name.

**Ross Musgrave** (MD '43), Distinguished Clinical Professor of Surgery and executive director emeritus of the Medical Alumni Association, welcomed students into his home for dinner and into his office for advice about life and careers. If a student had a big residency interview pending, Musgrave might prep him or her with mock interview questions or even go over proper appearance. (However, it appears he never recommended his signature lapel flower.) A problem-based learning classroom, where students tackle complex, real-world problems in small groups, was recently named in Musgrave's honor. It is the first PBL room with a namesake. —CB and CS

FOR MORE INFORMATION: 1-877-MED-ALUM  
Or [mhsf@ia.pitt.edu](mailto:mhsf@ia.pitt.edu).



## CLASS NOTES

### '40s

**Thomas Allen** (MD '43, Obstetrics & Gynecology Resident '44-'45, '48-'51) attended medical school during the Second World War, and had completed only one year of residency at Magee-Womens Hospital when he was sent to Bremerhaven, Germany, and made chief of obstetrics and gynecology, delivering the babies of soldiers' wives. When he returned to the Pittsburgh area, he began a private ob/gyn practice. As a resident, Allen had seen many women suffering excessive blood loss and infection after illegal abortions. He felt that they often received more attention from the police than from the doctors. Often they were unable to bear children, and some died. Allen became active in the Abortion Justice Association, a political action group in Pittsburgh, and won awards from the National Abortion and Reproductive Rights Action League of Pennsylvania and the Greater Pittsburgh Chapter of the American Civil Liberties Union for his courage and commitment to women's health. Though

he retired from his practice in 1995, he continues to work part-time at the Women's Health Clinic.

Like many newly minted MDs of the '40s, **Frank Mateer** (MD '44) returned from World War II and discovered that all the residencies were full. Mateer took a fellowship in physiology, working with Pitt Professor Thaddeus Danowski, who was treating nephrosis with steroids effectively. But when they saw Westinghouse's artificial kidney, Danowski charged Mateer with investigating the new machine. In 1950, Mateer dialyzed his first patient; by 1954 he had used the machine on 150 cases of acute renal failure. Mateer developed Western Pennsylvania Hospital's dialysis department. He was one of the first physicians to use the experimental artificial kidneys, but he says he gained the most recognition when he dialyzed Liberace after the famed pianist inhaled the dry-cleaning solution he was using to clean one of his flamboyant costumes. Since retiring in 1999, Mateer has been remodeling his home and enjoying some of the rare first edition books in his collection.

### '60s

**John Godleski** (MD '69), associate professor of pathology at Harvard Medical School, fondly remembers participating in the School

of Medicine's summer research program, where he gained experience in pathology before entering medical school. Godleski, director of the Pulmonary Pathology Unit of Brigham and Women's Hospital and codirector of the Environmental Protection Agency/Harvard Center on Ambient Particle Health Effects, is working on the role of minute parti-

cles of air pollution in the development of diseases like heart disease, lung cancer, and asthma. His research indicates that the principal target organ of these particles is the heart.

### '70s

At officer basic training, it rained constantly as **Gary Brickner** (MD '75) learned how to handle weapons, call in medical evacuation helicopters, and put on a gas mask in nine seconds flat. Brickner is an obstetrician and gynecologist by training, but his job in the New Jersey Army National Guard is reminiscent of his intern days in the emergency room. As battalion field surgeon assigned to the 2nd Battalion, 102nd Armor Regiment, in Port Murray, N.J., he oversees efforts to stabilize soldiers in the field. As brigade surgeon for the 50th Brigade, 42nd Division, Brickner supervises all medics and physicians and ensures that 7,500 soldiers are medically fit for battle.

**Barbara Brandom** (Intern '76-'77, Anesthesiology Resident '77-'79, Pediatric Anesthesiology Resident '79-'80), professor of anesthesiology at Pitt and director of the North American Malignant Hyperthermia Registry at Children's Hospital of Pittsburgh, studies malignant hyperthermia (MH). MH is a rare, but potentially dangerous condition, which occurs when susceptible people receive inhalation anesthesia. Those who suffer from the disease have too much calcium in their muscles, which causes very high levels of acid and carbon dioxide during an attack of MH. Brandom has explored how best to treat children who undergo MH episodes during surgery. She's also looking at the everyday implications for people who are susceptible to MH. A few years ago, she heard about a high school football player who ran off the field, breathing quickly, with a slight fever. The trainer, thinking the player was hyperventilating, gave him a bag to breathe into, but because the athlete was MH susceptible, his pH levels became elevated, and he suffered cardiac arrest. Brandom is working with others to develop a genetic test to identify those who are susceptible to MH to avoid tragedies like this.

**Alvah R. Cass** (MD '76) is training for the 2004 Texas Special Olympics in power lifting with his son who has Down syndrome. The father-son team hopes to beat their personal best and lift a combined weight of 1,200 pounds. When Cass isn't at the gym or in the woods (he's an assistant scout master of his son's Boy Scout troop), he can be found at the University of Texas Medical Branch in Galveston. As director of research, vice chair, and tenured associate professor in the Department of Family Medicine, Cass develops techniques that will help primary care practitioners better screen their patients for disease. One such technique uses digital photography and reveals unusual blood vessels, tears, and hemorrhages of the retina that are indicative of diabetic retinopathy.

When **Andrew Kofke** (MD '78) was a resident at Massachusetts General Hospital, one of his patients suffered from a seizure disorder. As he monitored the patient, he realized that anesthesia seemed to contribute to the seizures. Thinking about that case eventually led Kofke to investigate neurotoxicity. While he was on the faculty at the University of Pittsburgh in the 1990s, he found that narcotics had the potential to cause seizures and brain damage in lab animals. As a professor at the University of

## MEDICAL ALUMNI ASSOCIATION OFFICERS

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Pennsylvania, he researches the connection between anesthetics and Alzheimer's disease. Kofke speculates that if anesthesia is administered multiple times to someone who is susceptible to Alzheimer's, that person is more likely to develop the disease at a younger age.

In the early 1980s, **Kathleen Downey** (MD '79) lived in Auckland, New Zealand, joining physicians on house calls, aiding midwives at births, working in the ER, and seeing patients in a family practice. She was interested in how New Zealand's socialized healthcare system differed from the system in the United States. That experience, coupled with stints in Bethel, Alaska, and on a Navajo reservation with the late Pitt Professor Ken Rogers, "opened her eyes," she says: "You can't assume that everyone you deal with has the same beliefs about their body and health care." As an associate clinical professor of family medicine at the University of Cincinnati and assistant director of residency training at the Wyoming Family Practice Center, Downey encourages cultural sensitivity in her students. She and her family host international college students, and Downey helps train students for the international medicine track at the university.

## '80s

**Edward Friedman** (MD '85,

Psychiatry Intern '85-'86, Psychiatry Resident '86-'89), associate professor of psychiatry at Pitt, earned undergraduate and graduate degrees in English language and literature. Friedman viewed literature as an information system and was interested in the way mental states could be induced by writing. While his wife attended dental school at Columbia University, Friedman met many psychiatrists and discovered that he shared their interests in cognitive systems. As he edited biology, sociology, and psychology textbooks at Random House, he overcame his fear of science and began a premed program. Friedman completed his MD at Pitt and continued his training in the Western Psychiatric Institute and Clinic. He is now the associate director of the Mood Disorders Treatment and Research Program and participates in resident education programs. With funding from the National Institute of Mental Health, Friedman evaluates the effectiveness of cognitive therapy in the treatment of mood disorders. In the next few years, Friedman will be working on the creation of the Bipolar Disorder Center for Pennsylvanians, which will be one of the first centers of its kind to treat manic depression.

**Earl Campazzi Jr.** (MD '89) says that he was so frustrated with managed care that he decided, "If I can't beat them, at least I can understand them." He received his MBA from Duke in 1999 and subsequently became chair of the operations research committee in preventive and occupational medicine at the Mayo Clinic. Now, he is comparing different ways to enter medical record data to determine which is most efficient.

## '90s

After **Daniel Medalie** (General

Surgery Resident '91-'94, Plastic Surgery Fellow '96-'99) graduated from Harvard with biology and anthropology majors, he studied art for a year, and then started medical school. Friends and family advised him to pursue a career in plastic surgery—what they saw as the perfect

combination of art and medicine. But he wasn't sure about plastic surgery until he trained at the Boston Shriners Hospital with Pitt's own Robert Goldwyn (Plastic Surgery Resident '61-'63). He is now an assistant professor of plastic surgery at Case Western Reserve University and chief of plastic surgery at Cleveland's VA hospital. He plans to resume researching less invasive reconstruction measures like adipose flaps, in which doctors take subcutaneous tissue from a leg to reconstruct an ankle, rather than the more common practice of transplanting tissue from another part of the body. While it is not always as reliable, it is a better procedure for patients with multiple medical problems.

**Thomas O'Toole** (Intern '91-'92, Internal Medicine Resident '92-'94, Fellow '94-'96), assistant professor of medicine at Johns Hopkins University, researches methods to increase access to care among marginalized groups, specifically homeless substance abusers. When O'Toole was an intern, he saw that homeless patients were often admitted, treated, discharged, and later readmitted for the same problem. O'Toole helped establish the Birmingham Free Clinic on Pittsburgh's South Side; he was later involved in the creation of two other clinics. As the current medical director of First Step Day Hospital's substance abuse program, O'Toole provides medical care and substance abuse treatment for the homeless. He also assists with broader needs like housing and unemployment benefits. O'Toole is a national program officer for the Open Society Institute's Program on Medicine as a Profession, which is developing a national initiative to engage med students in community service and advocacy.

As associate residency director for community programs, **Richard Pan** (MD '91) works with pediatric residents at the UC Davis Medical Center in Sacramento to help parents create healthy environ-



*The Hippocratean, 1995*

ments for their children. His residents go to parks and community centers to teach parents about children's health and explain how to ask good questions at the pediatrician's office. Pan was recently elected to the Council on Medical Education of the American Medical Association. He says his desire to serve started when, as a medical student, he learned that physicians need to work together to be advocates for their patients.

**Neal Thomas'** (Pediatric Critical Care Medicine Fellow '95-'98) interest in lung disease peaked when his son was born with neonatal lung disease. Babies with this disorder often spend months on ventilators, which, in turn, can cause lifelong breathing problems, ranging from asthma to severe lung disease like bronchopulmonary dysplasia. Two years later, Thomas' son is healthy and 10 times his birth weight, and Thomas, an assistant professor of pediatrics at Penn State Children's Hospital in Hershey, is researching the genetics of surfactant proteins. These proteins come in four varieties and are found in the lung fluid that keeps air sacs open. Thomas hopes his study will provide a way to identify and treat children with a genetic predisposition for lung disease. He's also working on a Master of Science in Health Evaluation Sciences degree from Penn State. In his spare time, he coaches his older sons' T-ball and soccer teams and plays center field in two softball leagues. —CB, MH, and JM



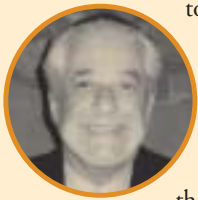
**THE WAY WE ARE: CLASS OF '64**

If you've spent much time in Pittsburgh, you know the legend: It was the bottom of the ninth in game seven of the 1960 World Series at Forbes Field when Bill Mazeroski blasted a home run over the left field wall, breaking a 9-9 tie with the New York Yankees and winning the championship for the Pirates. That moment is etched in

*continued on page 38*

Pittsburgh's collective memory; **Bernard Cohen** (MD '64) had tickets to that game. He begged and pleaded with his histology professor, Mel Hess, to change an exam that conflicted with the game. Hess refused, leaving Cohen with a tough choice. He passed the exam, but missed Maz's homer. Despite that heartbreak, Cohen, president of his class for three years, is thankful that he had such "awesome" clinical teachers. For 32 years, Cohen practiced plastic surgery in Pittsburgh; he retired from surgery in 2001. Today he is an assistant clinical professor of plastic surgery at Pitt.

Cohen's classmate **Edwin Morgan** (MD '64) has fonder memories of Forbes Field. Morgan's father was a *Pittsburgh Press* photographer, covering the Pirates and the Steelers. As a child, Morgan would help carry his dad's cameras onto the field, where he watched the games. Morgan became a team physician for the Florida Marlins baseball team, including the '97 World Series champions. The most striking Marlins' medical problem? A



Cohen



Morgan

team outbreak of mumps. In 2001, Morgan retired as director of the University Health Service at West Virginia University, where the professor emeritus was instrumental in developing programs such as mental health/psychiatry, family planning, and alcohol and drug education for students. He also has been a visiting professor in Wales, Germany, and Zimbabwe. Morgan, who specialized in pulmonary medicine, found Zimbabwe especially challenging because of the prevalence of tuberculosis and silicosis. He looks forward to catching up with classmates at the upcoming reunion in May.

**Alex Azar** (MD '64) is a big fan of a certain Olympic gold medalist in women's soccer and a former Baltimore Orioles player—they happen to be his stepchildren.

Azar recalls scrubbing in with Henry Bahnson, the late chair of the surgery department. One day, Bahnson was repairing an abdominal aneurysm. As Azar held the retractor, the patient began bleeding. Bahnson calmly put his finger over the wound and started a lecture about how the body stops bleeding on its own. Azar has worked for more than 25 years as an ophthalmologist. In 1997, he founded the Azar Eye Institute. He also teaches part-time at Johns Hopkins University. —CB

## ROBERT SHALER ON EMOTIONAL DISTANCE

BY HATTIE FLETCHER

For Robert Shaler, using DNA to identify a homicide victim has become fairly routine. It's a scientific process divorced from emotion, ending with the satisfaction of a match.

But after September 11, 2001, emotional distance became impossible. Shaler, who completed his biochemistry postdoc at the School of Medicine in 1970, is director of forensic biology in the Office of the Chief Medical Examiner of New York City. The 20,000 human remains from the World Trade Center are ultimately his responsibility to identify. Using DNA provided by family members, he and his staff have made positive matches for 1,534 out of the 2,792 victims so far.

He knows that some will never be identified. The DNA is so damaged in many of the remains that standard identification is impossible. But his staff has pushed the science to where they are able to match DNA from strands that are only 50 to 85 base pairs long, compared to the usual 200 to 400 base pairs. The families they've come to know are the constant reminders of why his staff members push so hard. When the grieving families would descend upon the medical examiner's office, Shaler would meet with them weekly, sometimes more often, and explain everything his staff was doing to help them. It was impossible not to share in their grief or want to work harder for them. His coworkers sometimes wept openly as they went about their jobs.

Shaler partly blames the stress of the job for the heart attack he suffered last May, but he has no regrets about the path he started on when he saw an ad for a course in scientific sleuthing at Pitt. Regarding his lab's task after September 11: "It's nothing anyone in their right mind would choose to do. But it [is] a tremendous honor to work for these families."



Shaler's job is to identify remains from the World Trade Center attack.

## IN MEMORIAM

### '40s

**WILLIAM OSHEKA**  
(MD '43B)  
NOVEMBER 3, 2003

**PEGGY JANE BLYTHE**  
(MD '44)  
SEPTEMBER 12, 2003

### '50s

**THOMAS LLOYD WILLIAMS JR.**  
(MD '52)  
SEPTEMBER 26, 2003

**DONALD W. GAYLOR**  
(MD '54)  
OCTOBER 13, 2003

**HERBERT G. KUNKEL**  
(MD '54)  
AUGUST 2, 2003

### '60s

**WILLIAM A. STONE**  
(MD '62)  
SEPTEMBER 14, 2003

### '70s

**MICHAEL FLYNN**  
(MD '76)  
NOVEMBER 14, 2003

NOTE: THE AMERICAN MEDICAL ASSOCIATION, A PRIMARY SOURCE FOR DEATH NOTICES OF OUR ALUMNI, NO LONGER PRINTS AN OBITUARY LIST. WE ENCOURAGE YOU, MORE THAN EVER NOW, TO LET US KNOW ABOUT ALUMNI WHO DIED RECENTLY. (ON THE INSIDE FRONT COVER YOU'LL FIND CONTACT INFORMATION FOR THE MAGAZINE.)



## FOR THE PEOPLE: BRUCE DIXON

BY MEGHAN HOLOHAN

In November 1995, a 19-year-old Robert Morris College student was life-flighted to UPMC Montefiore. They rushed him to the ICU. He was in critical condition, burning with a fever. Bruce Dixon (MD '65) was driving home on the turnpike from a weekend trip when he got the call. "I'll be there," he said.

It was late when Dixon, the director of the Allegheny County Health Department, arrived in the ICU. He sat down with the boy's family, explaining that their son was suffering from meningococcal meningitis; the 28th victim of the disease that year. As Dixon tried comforting the family, he had no idea that the boy would die—the fourth death of the outbreak.

Joan McMahon, who has spent her entire professional life in public health and is the chief of the county's infectious diseases unit, is still impressed when she sees Dixon at a patient's bedside or leading a community meeting in a high school gym.

"He believes in bringing public health to where the people are. He's very approachable—he's out in the community," she says.

Yet Dixon, who has led the Allegheny County Health Department since 1992, is known more for his willingness to confront public health problems than he is for his bedside manner. He recently rallied to ban smoking in restaurants, even after several statewide bills prohibiting smoking in restaurants had failed. Dixon announced his plans, then restaurateurs in Pittsburgh balked at the proposal, claiming their businesses would suffer. The ban was about to go into effect when at the last moment the tobacco and restaurant lobbies blocked the initiative.

Dixon stops to sit at a local bakery and outline the need for the ban; he still gets energized by the thought of it being implemented one day. This is how he approaches most issues: He works through the problem in earnest. And he seems to thrive under scrutiny. Early in his tenure, the health department's restaurant inspections were being criticized; so Dixon

made inspections more exhaustive. In 1993, when Pittsburgh's infant mortality rates were higher than the rest of the country's, Dixon helped organize the Healthy Start program in neighborhoods with the highest number of deaths. That program has helped reduce the number of African American infant deaths in those neighborhoods by 50 percent.

When Dixon walks, he walks briskly; he is a man with a destination. And he's always late. (Though that doesn't stop him from pausing to chat with scared-looking patients in the STD clinic or dropping by a renovated office to check the freshly painted walls and ask the nurses if they are happy with the change.)

As forthright as Dixon is about public health, he was hesitant to take the director's position at all—he was afraid he wouldn't be able to continue to teach rounds.

As an internal medicine intern in 1976, Gregory Fino (MD '76, Res '80, Fel '82) came into UPMC Presbyterian one night, expecting, like every other night, to see the second-year resident who was his mentor. Instead, Dixon met him. The resident was sick, so Dixon, an attending, took the resident's place, helping the young intern with rounds.

"It was unbelievable that an attending would do that," says Fino, codirector of critical care medicine at St. Clair Hospital.

Fino, who was chief resident under Dixon from 1979 to 1980, recalls calling Dixon in to see a patient who had Laurence-Moon-Biedl

syndrome. This is a rare disease that starts in childhood and often causes children to have a sixth finger, which is normally removed, as was the case with this patient. The residents didn't tell Dixon any of the patient's history, but Dixon strolled over to the patient, looked at his hand, and said, "One finger is missing. It's Laurence Moon Biedl."

"Bruce Dixon is the smartest physician I've ever worked with and will ever work with," notes Fino.

Like his mentor, Pitt Professor Jack Myers, Dixon enjoys teaching most. When his friend Mark Richards was director of the health department in the 1970s, he asked Dixon to head the STD clinic and program. Dixon reluctantly agreed. Soon after, he launched one of his unconventional public health initiatives.

Legend has it that the lanky crew-cut Dixon used to dash into brothels, giving everyone STD tests to prevent the spread of venereal disease. The legend isn't entirely true. Dixon set up clinics in brothels, he explains with characteristic clinical delicacy: "A fair number of people used their services, and we didn't want people to get infected satisfying base instincts." And when HIV started showing up in Pittsburgh, Dixon, along with other Pitt professors and doctors, worked with the community to slow the spread of the disease.

Decades later, it's not unusual to hear other physicians engaged in local outreach work use this word when describing Dixon: Hero. ■



Dixon



"First do no harm" was good advice. But this looks like a case of too much of a good thing. If you could let us know who these men are and what they're trying to accomplish, we'd be indebted, or at least grateful, to you. See the magazine contact information on our inside front cover.



# CALENDAR

## OF SPECIAL INTEREST TO ALUMNI AND FRIENDS

### CLASS OF '59 REUNION MARCH 13-19

Lago Mar Resort and Club  
Fort Lauderdale, Fla.  
For information:  
Richard Finder, MD '59  
954-925-7461  
rfinder320@aol.com

### BAHNSON LECTURE MARCH 27

10 a.m.  
Scaife Hall, Lecture Room 5  
Andrew S. Wechsler, MD, Speaker  
For information:  
Kathleen Haupt  
412-647-5314  
www.surgery.upmc.edu

### DONALD S. FRALEY MEMORIAL GRAND ROUNDS

APRIL 16  
8 a.m.  
Scaife Hall, Lecture Room 6  
Joseph G. Verbalis, MD, Speaker  
"Understanding Hyponatremia:  
A Pathophysiological Approach"  
For information:  
Felicia Emanuel  
412-648-9647

### MINORITY ALUMNI WEEKEND

APRIL 16-18  
For information:  
Office of Minority Affairs  
412-648-8987  
minorityaffairs@medschool.pitt.edu  
or Medical Alumni Association \*

### PITT MED GOLF OUTING APRIL 24

8:30 a.m.  
Quicksilver Golf Club  
Midway, Pa.  
For information:  
Ronald Tribble  
412-648-9090  
rptst7@pitt.edu

### BLACK BAG BALL \*

APRIL 30  
Marriott City Center  
Pittsburgh

### AAMC NORTHEAST GROUP ON EDUCATIONAL AFFAIRS REGIONAL MEETING

APRIL 30 & MAY 1  
University of Pittsburgh School of Medicine  
Alumni Hall  
For information:  
Office of the Vice Dean  
412-648-9000  
vicedean\_staff@medschool.pitt.edu  
www.omed.pitt.edu/pittmed/negea

### STARZL LECTURE

MAY 1  
10 a.m.  
Scaife Hall, Lecture Room 5  
Norman Shumway, MD, Speaker  
For information:  
Kathleen Haupt  
412-647-5314  
www.surgery.upmc.edu

### SCOPE AND SCALPEL

MAY 21 & 22  
The Antonian Theatre, Carlow College  
Pittsburgh  
For information:  
www.scopeandscalpel.org

### MEDICAL ALUMNI WEEKEND 2004 \*

MAY 21-23

#### Classes Celebrating:

1939	1969
1944	1974
1949	1979
1954	1984
1959	1989
1964	1994

### SENIOR CLASS LUNCHEON \*

MAY 21  
Twentieth Century Club  
Pittsburgh

### ALUMNI BREAKFAST & ALUMNI DINNER \*

MAY 22  
Sheraton Station Square  
Pittsburgh

### GRADUATION CEREMONY

MAY 24  
10 a.m.  
Carnegie Music Hall  
Pittsburgh  
For information:  
Student Affairs Office  
412-648-9040  
student\_affairs@medschool.pitt.edu

\* Medical Alumni Association-  
sponsored event

For information: 412-648-9090  
or 1-877-MED-ALUM  
medalum@medschool.pitt.edu

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



## THE LEGEND LIVES

Fifty years ago, two different musical sensations debuted within months of each other—Elvis Presley and Scope and Scalpel. But which of the two performances did Frank Sinatra describe as “a rancid-smelling aphrodisiac,” which fosters “destructive reactions in young people”? We’re not telling. (But we’re pretty sure he had the wrong one.)

**Scope and Scalpel’s 50th  
Friday & Saturday, May 21 & 22  
Reception Saturday**

Contributions are being accepted to make this the best show ever.

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